National Cancer Center, Japan

Center for Promotion of Translational Research (**CPOT**)

CPOT Research Seeds Catalogue 2023

国立がん研究センター 橋渡し研究推進センター
National Cancer Center
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CPOT Research Seeds Catalogue

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National Cancer Center (NCC) Japan / CPOT seeds

Investigation of non-clinical study items for an antigen-presenting cell platform for cancer therapy

Yasushi UEMURA, DDS. Ph.D.
Lab Head, Cancer Immunotherapy/EPOC/NCC

CPOT #21-preF-02

Vision

- Aiming to develop cancer immune cell therapy.
- In recent years, "cancer immunotherapies" such as CAR-T cell therapy and immune checkpoint inhibitors have been put to practical use. The future challenge is to overcome "solid tumors" for which CAR-T cell therapy is not indicated and "cancers" that are resistant to immune checkpoint inhibitors. This seeds will widely provide immune cell therapies for these cancers.

Innovation

- The universalization of the cells by eliminating unnecessary HLA antigens allows them to be universally administered as antigen-presenting cells for cancer therapy.
- Although derived from iPS cells, they can be grown at the end-product stage, enabling mass production and eliminating the need to induce differentiation each time, giving them an international competitive advantage in terms of quality and manufacturing cost.
- The ability to target intracellular cancer antigens makes it widely applicable to the treatment of cancers for which CAR-T cell therapy is not indicated.
- Induces T-cell infiltration into cancer tissue, making it applicable to the treatment of cancers resistant to immune checkpoint inhibitors.

Partnering

【Expected partners】

Pharmaceuticals

CDMO

【Expectation】

Investigational drug manufacturing and conducting clinical trials

Research Outline

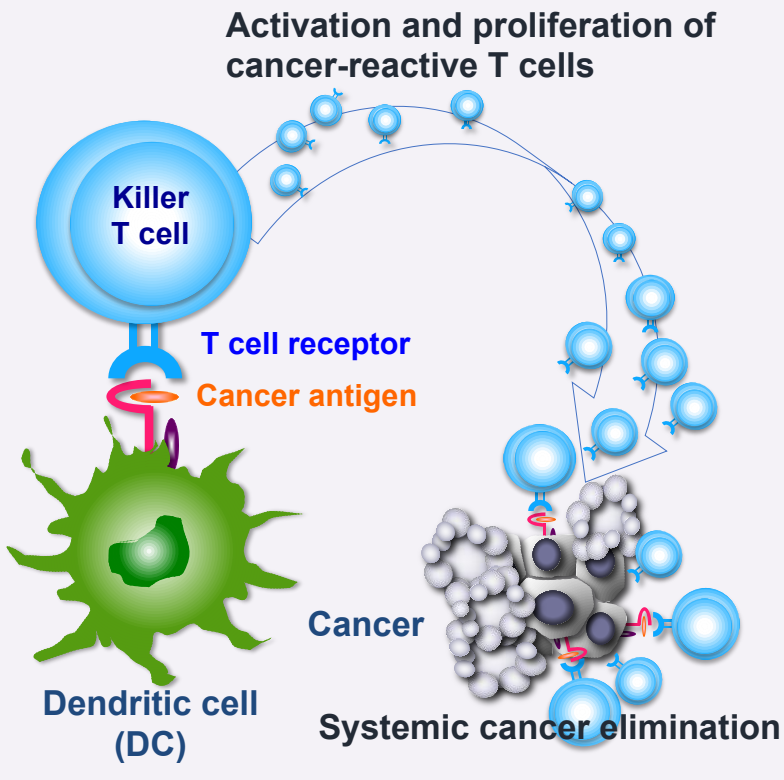
Key Words: #iPS cell, #Immune response, #Cancer Immunotherapy

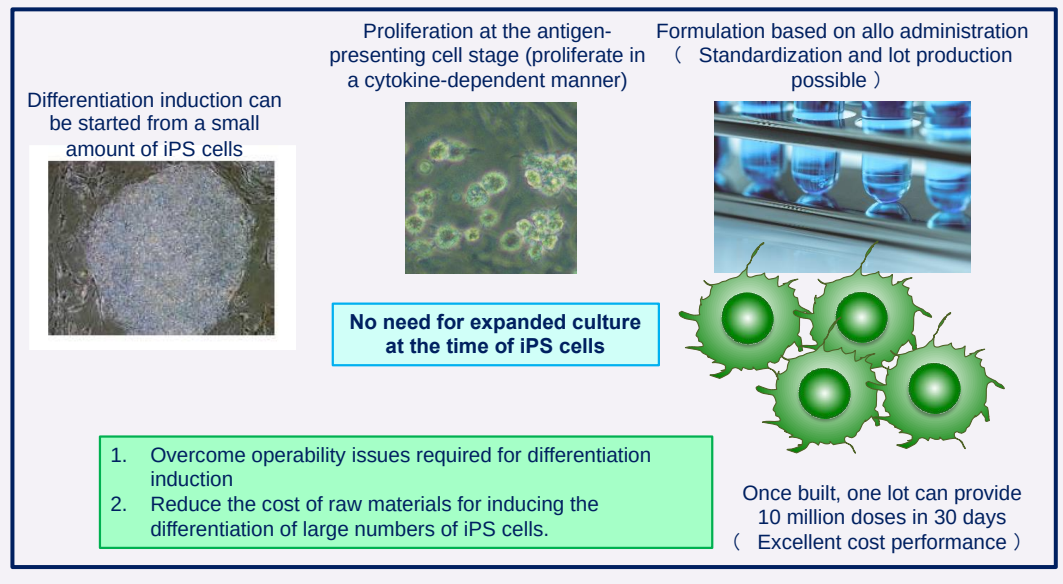
Dendritic cells (DCs) express many molecules that act as gas pedals to promote an immune response and are most adept at stimulating T cells.
Cellular therapy in which DCs are loaded with cancer antigens is one of the most effective therapies.

However, there are problems with DC progenitor cells, such as the inability to obtain a sufficient amount of DC progenitor cells through patient blood collection and the inability to obtain stable efficacy due to quality instability.

We have constructed DC-like antigen-presenting cells from other iPS cells that are capable of growth control using cytokines and have better clinical efficacy than autologous DCs.
This system has the following advantages.

1. non-self-directed iPS cells (Quality Stability)
2. Versatility through universalization (Destruction of unnecessary HLA)
3. Enables mass production (can be multiplied in the final product))
4. Lower cost (lot production possible)
5. Improved efficacy through genetic modification





PCT/JP2021/18121 (2021.5.13)

National Cancer Center (NCC) Japan / CPOT seeds

Development of a Minimally Invasive Treatment for Adhesive Small Bowel Obstruction

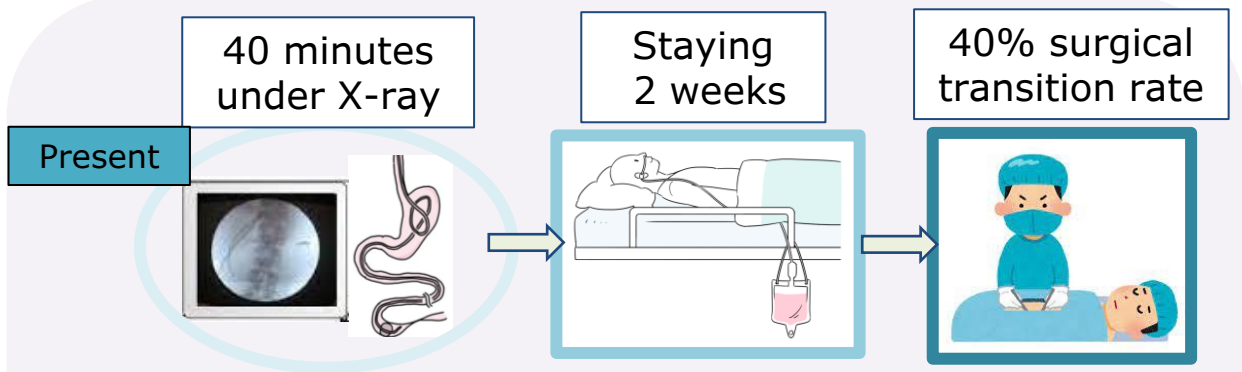
Hironori SUNAKAWA, MD.
Doctor, **Gastrointestinal Endoscopy Dept.**/
Hospital East/NCC

CPOT #21-A-16

Vision

- OBJECTIVES
  To develop a new minimally invasive therapeutic device device that will decrease the rate of surgical conversion for patients with adhesive small bowel obstruction (SBO).
- Medical Needs/Problems to be Solved
  Insertions of an ileus tube (3-4 m long, 6 mm width) are used to treat SBO. Despite the significant patient pain and long hospital stay, the surgical conversion rate is as high as 40%. Surgical procedures can release adhesions, but surgeons prefer to avoid open surgery because of the possibility of creating new adhesions. These challenges call for minimally invasive and highly effective treatment of SBO.

Innovation



*Disclosed after CDA is signed.

Partnering

[Industries interested in collaboration]

Medical/Institutional

Machinery/Equipment

Medical/Diagnostic/Analytical (Equipment)/Venture Capitals

[Expectations for collaboration]
Medical device development, conducting clinical trials, and start-up support

Research Outline

Key Words: #Medical devices and equipment, #Small bowel obstruction (SBO)

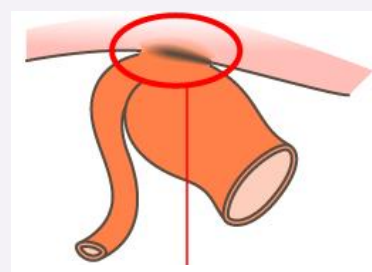
Etiology of SBO [1~3]

- **Adhesion** 60%
- Cancer
- Hernia
- The others

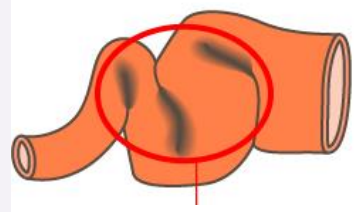
Main causes of adhesions

Abdominal surgery

1.Miller G, et al. Gordon PH. Am J Surg 2000; 180:33.
2.Bizer LS, et al. Surgery 1981; 89:407.
3.Lawal OO, et al. S Afr J Surg 2005; 43:34, 36.

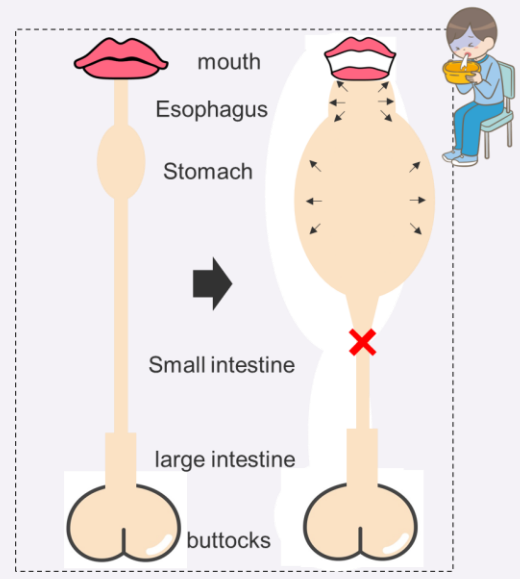


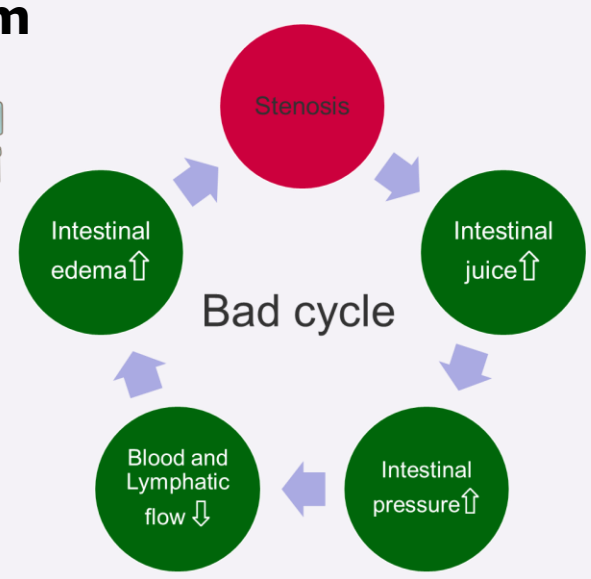
Case of adhesion between small intestine and abdominal wall



Case of adhesion between small intestines

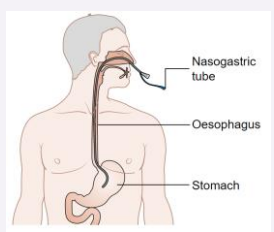
Disease mechanism



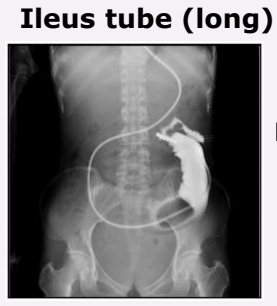


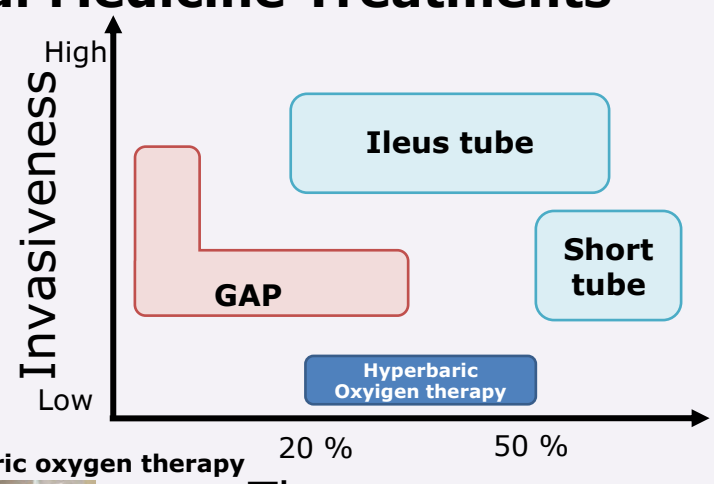
Existing Internal Medicine Treatments

Gastric tube (short)



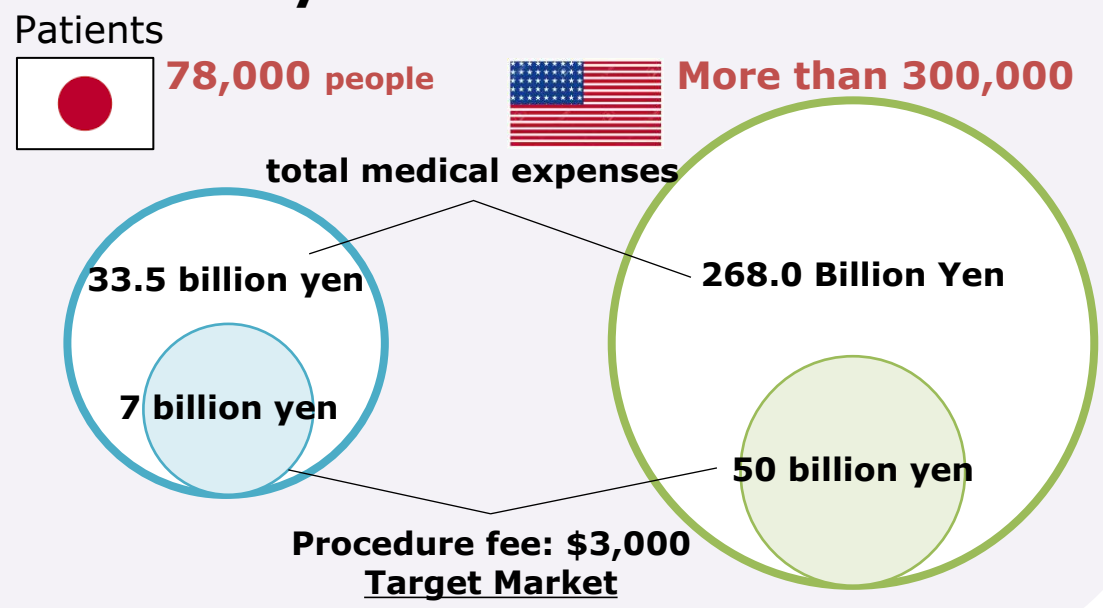
Ileus tube (long)





hyperbaric oxygen therapy

Market Analysis



*Disclosed after CDA is signed.

National Cancer Center (NCC) Japan / CPOT seeds

Development of tracheal intubation assistance device

Manabu HASHIMOTO, MD.
Chief of Dept., Anesthesiology Dept./
Hospital East/NCC

CPOT #21-A-31

Vision

- VISION
  We aim to improve the shortage of anesthesiologists through the development of tracheal intubation assistance device.
- OBJECTIVE / Medical needs
  Through this research and development, we aim to meet the following medical needs.
  1) Shortening the long-term training period by using machine learning
  2) Reduce the risk of infection caused by using conventional device

Innovation

[Novelty]
Currently, there are no reports from facilities that are looking to launch similar device development, so it can be said that it is a so-called blue ocean.

[Superiority]
At our facility, the development site and the clinical site are closely related, so feedback from the clinical side to the development side's prototype is smooth and prompt.

Partnering

【Expected partners】
Machinery/Device

【Expectation】
Patent application, Development of medical device, Implementation of clinical trials, Start-up support, etc.

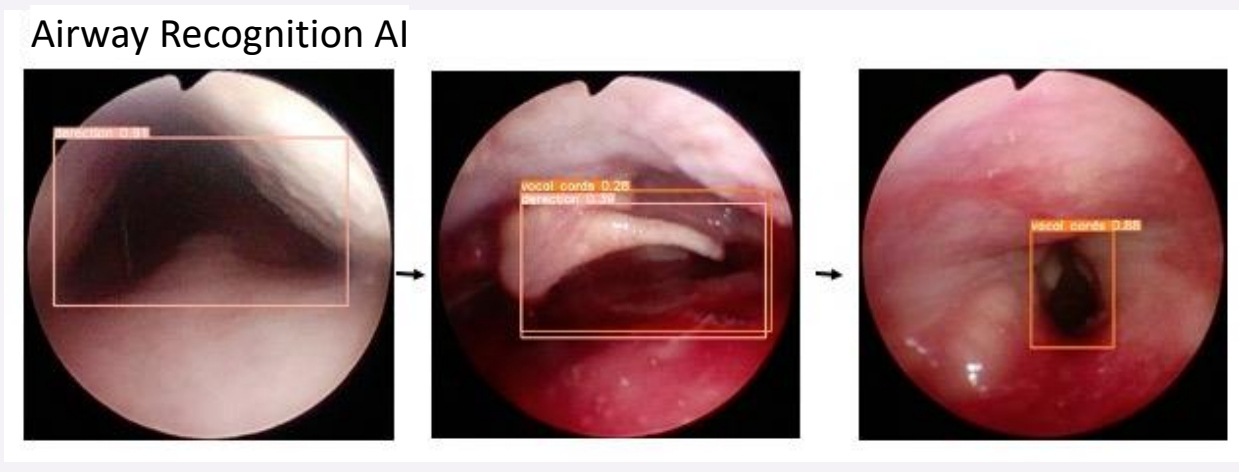
Research Outline

Key Words: #Medical Device, #AI

【Purpose】
Through the development of device that supports tracheal intubation, we aim to improve the situation of shortage of anesthesiologists and improve safety for both patients and medical staff.

【Background】
Fiberoptic intubation is a procedure used when tracheal intubation using a laryngoscope is difficult and is an important procedure for anesthesiologists even today when video laryngoscopes are commonly used. However, there are not so many opportunities to perform this procedure, and it can be said that it is a difficult procedure to acquire training.

【Current status】 *Details will be disclosed after the CDA is concluded.
We are proceeding with the development of the part that will be the eyes and the part that will be the arm during tracheal intubation.
AI technology based on deep learning was used for the visible part, and we succeeded in recognizing the respiratory tract from clinical images.
(Presented at the 70th Annual Meeting of the Japanese Society of Anesthesiologists)



National Cancer Center (NCC) Japan / CPOT seeds

Development of an AI system to assist in the diagnosis of superficial pharyngeal cancers

CPOT #22-A-18

Ryuichi HAYASHI, MD. Ph.D.
Deputy Director, Hospital East/NCC

Vision

- We aim to develop the AI system that supports the diagnosis of superficial pharyngolaryngeal cancer using pharyngolaryngoscopy .

- In the case of superficial pharyngolaryngeal cancer, detection could be achieved by the detail observation skills using a pharyngolaryngoscopy. This initiative involves integrating the AI system into the pharyngolaryngoscopy to aid in the diagnosis of pharyngolaryngeal cancer, aiming to contribute to early detection and improved patient survival.

Innovation

【Novelty】
There have been no previous reports of diagnostic supporting AI utilizing pharyngolaryngoscopy, indicating a high degree of novelty.

【Advantages】
Significant Dataset: Due to the high number of pharyngolaryngoscopy examinations and surgeries conducted for pharyngolaryngeal superficial cancers, we have the significant datasets.
Abundance of Images: Pharyngolaryngeal images captured via gastrointestinal endoscopy could be utilized as the training data.
High-Quality Annotations: Specialists in our institution could create the better labeled training data.
Leveraging Prior Research: The experience gained from previous studies involving the AI development using gastrointestinal endoscopy could be applied effectively.

Partnering

【Expected Partner】
Medical institute
IT, Electronics/Digital
Machinery/Device
Medical/Diagnosis/Research Devices
Software for Diagnostic Imaging

【Expectation for the collaboration】
Joint development for the business, Join patent application, Pre-clinical studies and Clinical studies

Research Outline

Key Words: #Diagnostics , #Medical Devices & Instruments, #AI

【Current Status】
In recent years, advancements in the development of gastrointestinal endoscopic equipment and diagnostic techniques have enabled early detection of superficial pharyngolaryngeal cancers. Similarly, through pharyngolaryngoscopy examinations performed by otolaryngologists, superficial cancers could be detected and diagnosed using Narrow-band imaging (NBI) [1]. However, the diagnostic capability for superficial pharyngolaryngeal cancer remains limited, and there is a significant demand for AI systems to support the diagnosis of superficial pharyngolaryngeal cancer, especially in clinics and otolaryngology departments overseas where the observation using NBI may not be widespread.

While there have been reports of AI diagnostic model construction based on gastrointestinal endoscopic images [2], reports of AI systems supporting pharyngolaryngeal cancer diagnosis using pharyngolaryngoscopy images are lacking.

【Objective】
Our aim is to develop the AI system that assists otolaryngologists in diagnosing pharyngolaryngeal cancer using videoscopes, ultimately contributing to early detection and improved patient survival.

【Reference】
1) Muto, et al. (2010) J Clin Oncol 28: 1566-72.
2) Inaba, et al. (2020) Head Neck 42: 2581-2592.

【Unique sales point for the patents】
・The number of patents application：12（Year 2022）
・There have been no previous patents of diagnostic supporting AI system utilizing pharyngolaryngoscopy so far.

National Cancer Center (NCC) Japan / CPOT seeds

Development of DDS for nucleic medicine

Hirofumi YAMAMOTO, MD. Ph.D.
Professor, Osaka University

CPOT #22-A-20

Vision

- Many nucleic acid (NA) medicines such as antisense oligo and siRNA have been developed, but problem is lack of useful drug delivery system (DDS) which carries NA to the target lesions.
- We have shown successful therapeutic efficacy by various NAs loaded on our DDS in mouse disease models.
- In this project, we produce and provide a novel DDS indispensable to cure metastatic tumors by repeat treatments in a short period (2 weeks to one month).

Innovation

- ✓ At present many DDSs carry NA (nucleic acid) not only to tumors but also to liver. Thus, cytotoxic NA cannot be used due to liver damage.
- ✓ Our DDS deliver NA to tumors but not to normal organs including liver, so cytotoxic NA is available to use.
- ✓ With our DDS, natural (non-modified) NA exerts a potent anti-tumor efficacy.
- ✓ This DDS is cheap in cost and safe, thus consecutive administration is possible.
- ✓ We can aim to cure metastatic stage IV diseases with this system.

Partnering

【Expected partners】

Pharmaceuticals

Medical institute

IT, Electronics/Digital

CMO/CDMO/CRO/SMO

【Expectation】

drug manufacture、clinical trial、business with experimental material、business in pet diseases

Research Outline

Key Words: #DDS, #siRNA, #microRNA, #cancer

- Our DDS delivers massive NA to tumors in mice compared with liposome（Fig.
- Injection of apoptosis-inducing NA on conventional DDS killed mice due to liver failure. With our DDS mice were healthy and no damage was noted in liver (Fig. 2).
- In contrast to conventional DDS, our DDS is devoid of accumulation of NA in normal organs(see red line, Fig. 3).
- Through support industry project we accomplished 30L-sized scale up of DDS (Fig. 4). 30x safety test was successful in monkeys.

Fig. 1 Comparison with Liposome

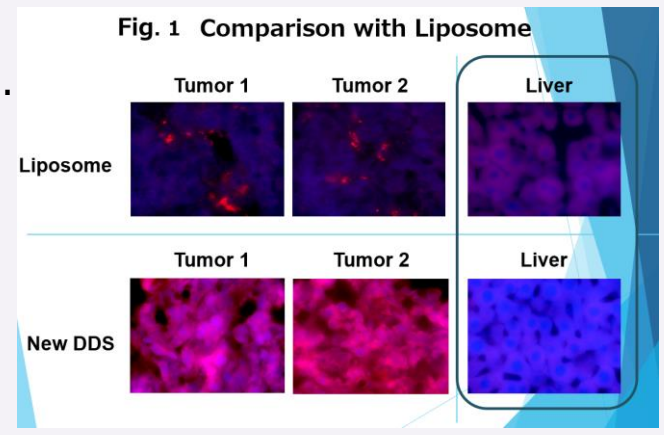


Fig. 2 Damage of LncRNA to liver

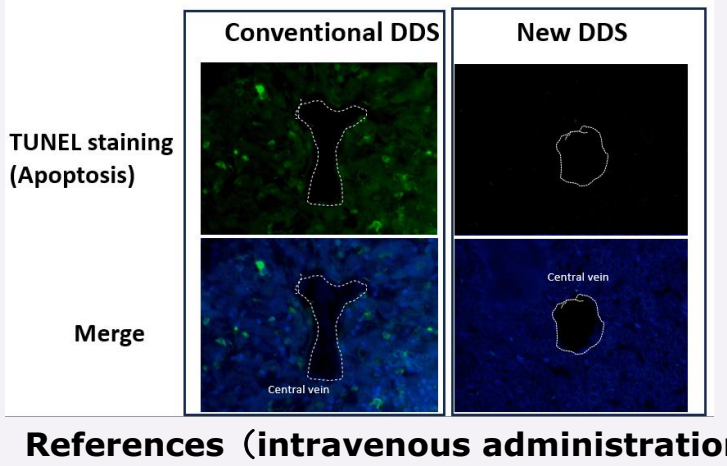


Fig. 3 Bioavailability of fluorescent siRNA in tumors and normal organs after i.v. injection into mice harboring HT29 colon cancer xenograft

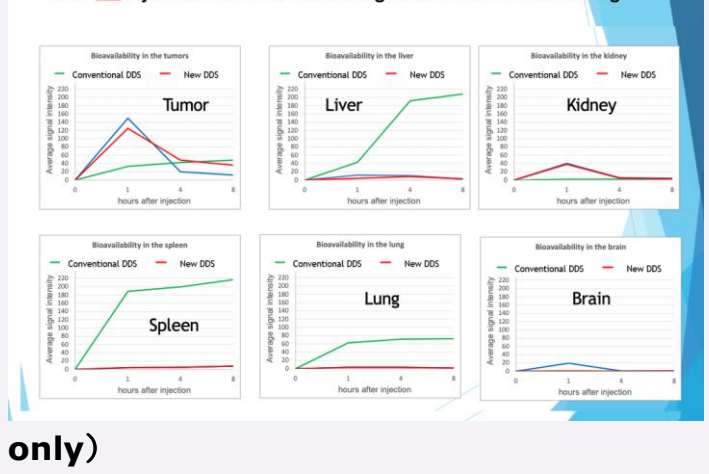
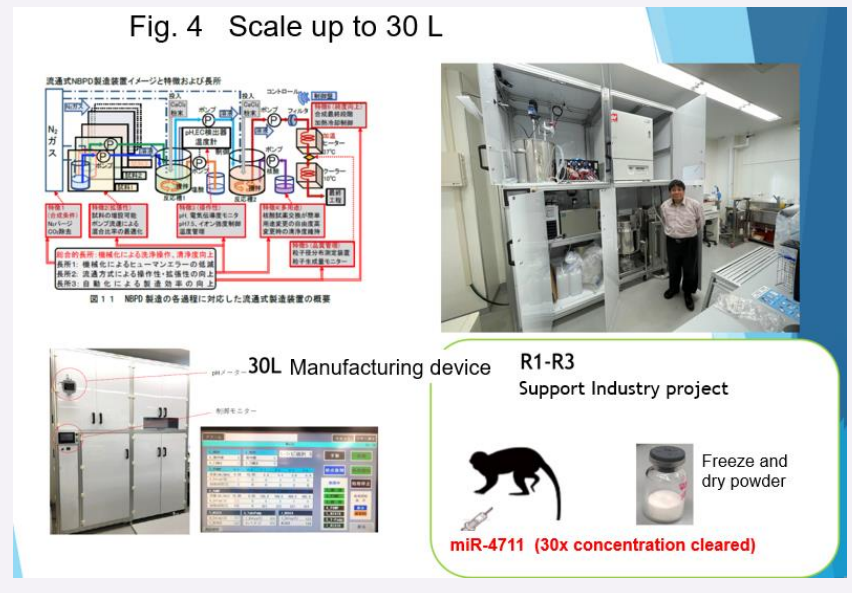


Fig. 4 Scale up to 30 L



References（intravenous administration only）

Wu Xin, et al. (2015) PlosOne 10: e0116022.
Takahashi H, et al. (2015) Mol Cancer Ther 14:1705-16. Takeyama H, et al. (2015) Mol Cancer Ther 13:976-85.
Ogawa H, et al. (2015) PlosOne 10, e0127119. Hiraki M, et al. (2015) Mol Therapy NA 4, e231.
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Takahashi H, et al.(2018) Frontiers in Immunology 9:783. Tamai K et al. (2018) Mol Cancer Ther 17: 1613-1622.
Morimoto Y, et al. (2020) Br J Cancer 122:1037-1049. Wu X, et al. (2021) J Pers Med 11: 1160.
Wang J, et al. (2022) Int J Oncol 60:13. Tsujimura N, et al. (2023) Pharmceuticals 16: 618.

National Cancer Center (NCC) Japan / CPOT seeds

Development of a novel cancer immunotherapy focusing on the biliary microbiota

CPOT #22-A-32

Shogo KUMAGAI, MD. Ph.D.
Project researcher, Division of cancer immunology/
EPOC/NCC

Vision

- Immune checkpoint inhibitor (ICI) therapy combined with chemotherapy is the standard treatment for advanced cholangiocarcinoma, but the efficacy needs to be enhanced.
- A multilayer omics analysis of cholangiocarcinoma surgical specimens was performed to identify the biliary flora that activate the anti-tumor immune response. The goal is to further elucidate the detailed mechanisms that lead to improved resistance to combined immunotherapy treatment. If we can demonstrate the feasibility of utilizing specific bacterial species in combination with ICI therapy, we expect to improve the prognosis of biliary malignancies.

Innovation

In considering novel cancer immunotherapeutic strategies for biliary tract malignancies, it is important to understand the multifaceted tumor microenvironment specific to biliary tract tumors. Most of the previous reports on tumor localization in biliary tract tumors have examined only tumor gene abnormalities or tumor-infiltrating immune cells, and there are almost no reports that have proposed therapeutic target factors based on detailed mechanical analysis of tumor localization as a whole network from various perspectives, including tumor genome abnormalities, comprehensive bacterial flora analysis, and immune response. There are almost no reports that have proposed therapeutic target factors.

Partnering

【Expected partners】

Pharmaceuticals

Medical institute

Biotech/Drug Discovery Service

Food/Beverages

Medical/Diagnosis/Research Devices

Venture capitals

【Expectation】

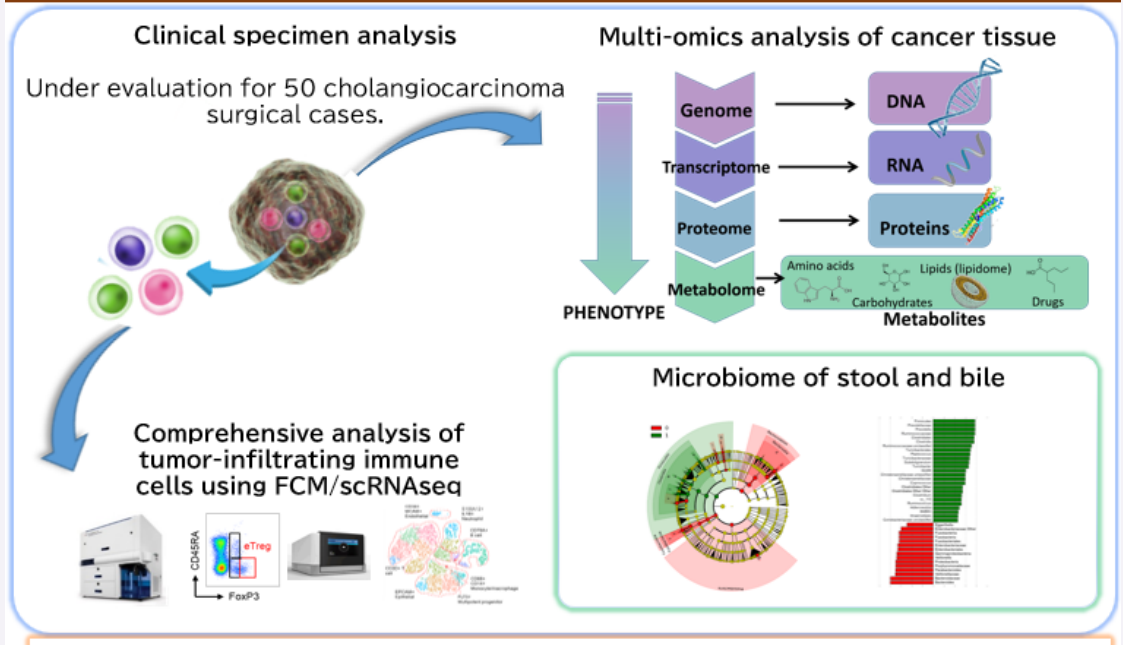
Joint patent application, running clinical trials, and start-up support

Research Outline

Key Words: #Biomarker, #Immune response, #Microbiome, #Metabolism

- Recently, the efficacy of immune checkpoint inhibitors (ICIs) in cancer therapy has been scientifically proven. However, there are many cases of resistance to ICIs, and the development of biomarkers to predict efficacy and therapies to enhance efficacy is needed. We have investigated the relationship between $CD8^+$ T cells, Tregs that suppress anti-tumor immunity, and oncogene abnormalities (Kumagai S, et al. Nat Rev Cancer 2021, Immunity 2020) and have continued to clarify the role of $CD8^+$ T cells and Tregs in the response to ICI We have continued to clarify the role of $CD8^+$ T cells and Tregs in ICI responses. We have analyzed fresh samples from patients treated with ICI and identified important immune phenotypes associated with ICI response (Kumagai S et al. Nat immunol 2020), which we have used as biomarkers in industry. In addition, we have the experimental technology to validate the association between organ-specific environments and immune responses (Kumagai S et al. Cancer cell 2022).

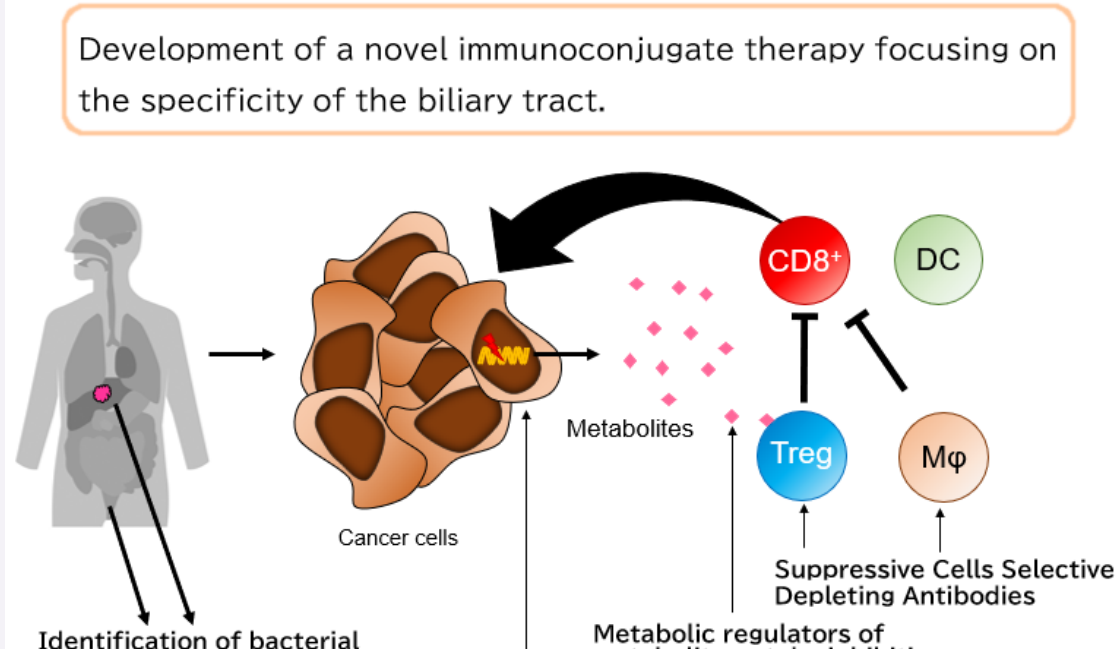
Research plan for current study



Integrated analysis of cholangiocarcinoma from four perspectives (immunology, genomics, metabolism, and bacterial flora) is conducted to elucidate the resistance mechanism of cancer immunotherapy.

Goals of Current Study

Development of a novel immunoconjugate therapy focusing on the specificity of the biliary tract.



National Cancer Center (NCC) Japan / CPOT seeds

Regenerative therapy for anal dysfunction using adipose tissue-derived stem cells

-multiple transplantation and scaffold tissue-

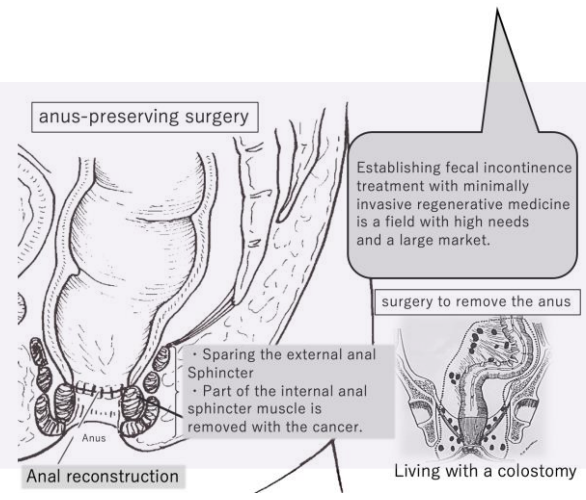
CPOT #22-A-46

Yuji Nishizawa MD, PhD
Colorectal Surgery Dept. & Quality Management/
Hospital East/NCC

Vision

➢ To provide regenerative medicine that improves anal dysfunction using autologous adipose tissue

➢ Currently, the only way to deal with severe anal dysfunction is to construct a permanent colostomy. The goal is to reduce the number of patients who become colostomy and reduce the degree of anal dysfunction to improve patient QOL.



Innovation

Regenerative medicine using cultured adipose stem cells, which can utilize a large number of adipose stem cells by collecting a small amount of autologous fat in a minimally invasive manner, is novel as a safe and highly effective treatment method. The aim is to research and develop more effective treatment methods using multiple transplantation, which are considered to be the great merits of treatments using cultured adipose stem cells, and adipose tissue as a scaffold. It will lead to the establishment of a treatment method that is superior in cost-effectiveness.

Partnering

【Expected partners】

Pharmaceuticals

Medical institute

Biotech/Drug Discovery

Venture capitals

【Expectation】

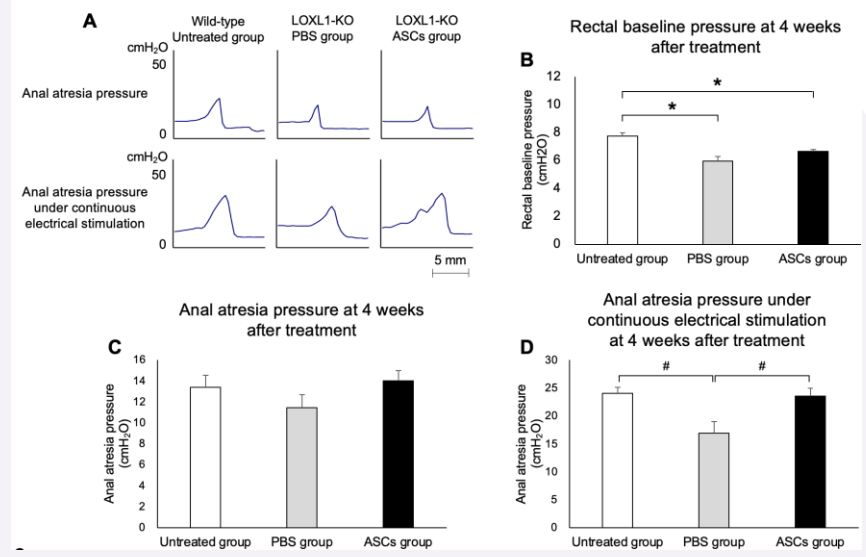
We hope to collaborate with companies that will participate in the cell processing and provision system for clinical practice

Research Outline

Key Words: #Somatic stem cells, #Anal dysfunction, #Rectal cancer, #ASCs

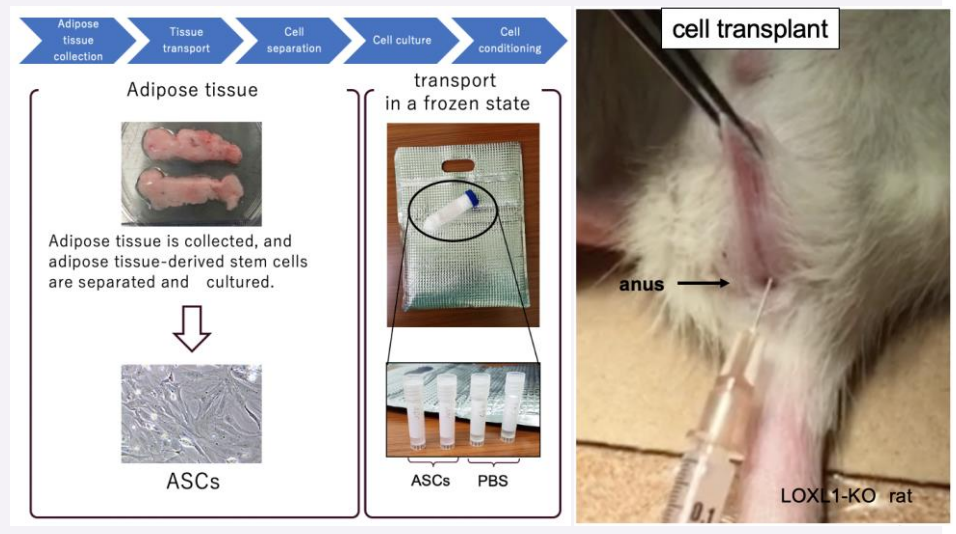
【 Postoperative anal dysfunction in rectal cancer 】

Colorectal cancer is the most prevalent disease. The 5-year survival rate for rectal cancer exceeds 70%. Anus-preserving surgery for rectal cancer has become popular, but the rate of postoperative anal dysfunction is as high as 80-90%, and patients are increasing year by year. There are potentially many patients with anal dysfunction, and the market for treatment of it is large.
It is expected that minimally invasive regenerative medicine will be established as a treatment for fecal incontinence.



【Our reserch】

LOXL1-KO (Lysyl oxidase like-1 knockout) rats were used as a fecal incontinence model. ASCs established from inguinal adipose tissue were transplanted into the anus at the 3, 6, 9 and 12 o'clock positions. Using SD rats as the control group, the anal leak point pressure under electrical anal stimulation was significantly higher in the transplanted group than in the control group 4 weeks after transplantation. Local transplantation of ASCs was found to enhance the effect of anal function.



【 This study and development 】

A cultured ASCs group and an ASCs + adipose tissue group will be compared to evaluate the effect of the scaffolding on the anal function. In addition, by transplanting ASCs and ASCs + adipose tissue twice each, we will compare the effect of anal function between the single-transplantation group and the multiple-transplantation group. Based on the scaffold and the number of times of transplantation, we will establish a new highly effective treatment method.

National Cancer Center (NCC) Japan / CPOT seeds

Development of novel nucleic acid drugs targeting the RdRP activity of hTERT

Mitsuhiro MACHITANI, Ph.D.
Staff scientist ,Division of Cancer Stem Cell,
NCC Research Institute

CPOT #23-S-07

Vision

Sarcomas are diverse malignant tumors arising from bone and soft tissue, and the development of treatment methods is expected. Since sarcoma cells do not have telomerase activity, the existence of the enzymatic subunit hTERT, has not been recognized in these cells. However, we found that hTERT exists across a wide range of cancer types, and that inhibition of the RdRP activity leads to an antitumor effect against non-epithelial malignant tumors including sarcoma. Furthermore, we have demonstrated that RdRP inhibition is effective against BRCAness cancers with mutations in the FANC/BRCA genes. In this study, we aim to develop a therapeutic method by inhibiting RdRP, based on the elucidation of the molecular mechanism of the RdRP activity of hTERT.

- We aim to develop a therapeutic method by inhibiting RdRP for sarcomas.
- We aim to develop a synthetic lethal therapy by inhibiting RdRP to treat tumors with FANC/BRCA mutations.

Innovation

- While cancer treatments targeting the reverse transcription activity of hTERT have been developed around the world, we focus on the RdRP activity of hTERT and aim to develop a novel cancer treatment that targets this RdRP activity.
- Targets the RdRP activity of hTERT in non-epithelial malignancies such as sarcoma, which are known to lack telomerase activity.
- We will develop a synthetic lethal therapy by inhibiting RdRP and FANC/BRCA genes.
- We confirmed that in these cancer cells, the anti-cancer effect of RdRP inhibition.

Partnering

【Expected partners】

Pharmaceuticals

Biotech/Drug Discovery Service

【Expectation】

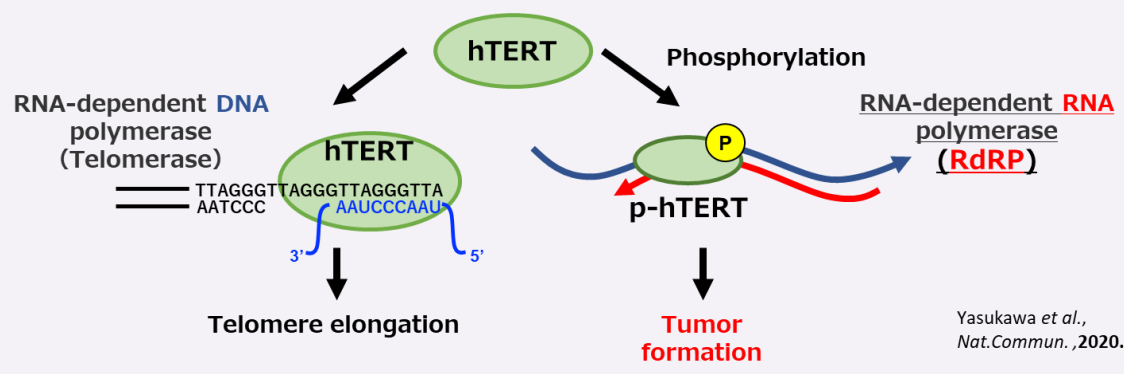
Joint patent application

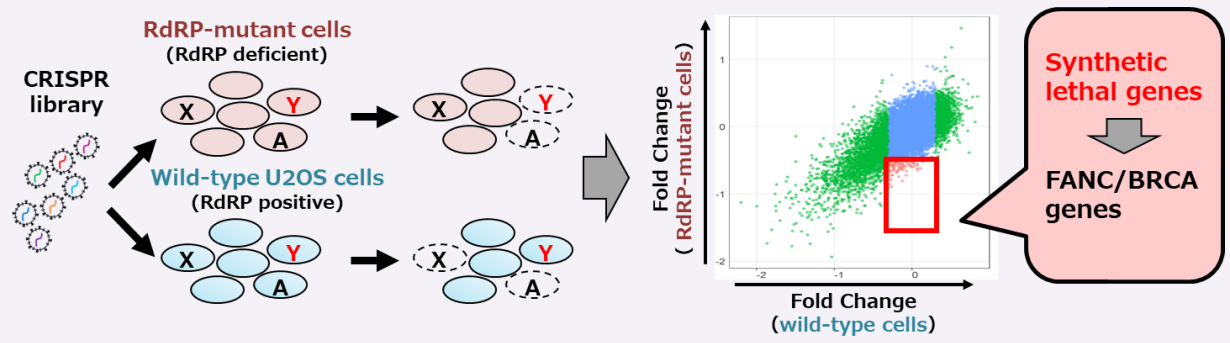
Research Outline

Key Words: #RNA, #Nucleic Acid Drugs, #hTERT, #RdRP

【Background】

We have found that phosphorylation of hTERT (p-hTERT) is essential for RNA-dependent RNA polymerase (RdRP) activity, and that RdRP activity of hTERT is associated with aggressiveness of various types of cancers (Nat Commun, 2020). Furthermore, we have recently discovered an expression of p-hTERT in malignant tumors derived from mesenchymal cells such as sarcoma, although these non-epithelial cancer cells do not have telomerase activity. p-hTERT exhibits RdRP activity but not telomerase activity in non-epithelial cancer cell. Loss-of-function of hTERT RdRP activity in such sarcoma malignant tumors leads to anti-tumor effects. In addition, using a genome-wide CRISPR loss of function screen, we identified genes in the Fanconi anemia (FANC)/BRCA pathway as synthetic lethal partners of hTERT RdRP. Mutations in the FANC/BRCA genes sensitized cells to inhibition of RdRP. Mechanistically, inactivation of RdRP and the FANC/BRCA genes led to accumulation of R-loop structures and induced DNA damage.





【Reference】

Yasukawa et al. (2020) Nat Commun 11(1):1557

【Aim】

In this study, we aim to develop a new method targeting RdRP for treatment of sarcomas and tumors with FANC/BRCA mutations.

National Cancer Center (NCC) Japan / CPOT seeds

Drug discovery for improvement of anti cancer-induced cardiotoxicity and pan heart insufficiency, focusing on the desacyl-ghrelin and its cognitive receptor-mediated signaling

CPOT #21-A-06

Yasuhito UEZONO, MD. Ph.D.
Researcher, Hospital East/NCC

Vision

- Anticancer drugs such as doxorubicin (DOX) exhibit 6-30% of cardiotoxicity, which worsen the quality of life of cancer patients.
- We discovered desacylghrelin (DAG) that was removed acyl residues from ghrelin and fail to bind to the ghrelin receptor, improved DOX-induced cardiotoxicity. Further, we identified a novel DAG receptor (DAGR).
- DAG/DAGR signals may improve heart failure through suppression of pathophysiological signals to cause heart failure.
- DAGR-activating compounds could be therapeutic seeds for improvement of heart failure, including DOX cardiotoxicity.
- Using a novel DAG/DAGR screening system, we already identified novel peptides that overcome endogenous DAG profiles.

Innovation

1) Only the applicant group has information on the novel DAG/DAGR pathway signaling.
2) We have information on the effects of DAG using DAGR-knockout cells and conditional knockout mice.
3) We constructed a screening system to identify DAG-like compounds through DAG/DAGR signals, and already identified compounds exceeding the properties of DAG.
4) Mode of Action (MOA) how DAG improves pathophysiol-ogical status of heart failure has almost been obtained.

As such, we have identified ① drug discovery targets required for licensing-out, ② developed a new screening method, and ③ novel peptides exceeding endogenous DAG. ④ We clarified MOA of DAG/DAGR signal.

Partnering

【Expected partners】

Pharmaceuticals・ Chemical

Drug Discovery Service

Venture capitals

【Expectation】

We would like to 1) do collaborative study from non-clinical stage sharing with the information of DAG/DAGR signaling,
2) co-apply for this patent and 3) complete non-clinical study and license it out.

Research Outline

Key Words: #Small molecule, #Biomarker, #Signal analysis, #Drug development, #Supportive care

【Background】

Anticancer drug DOX

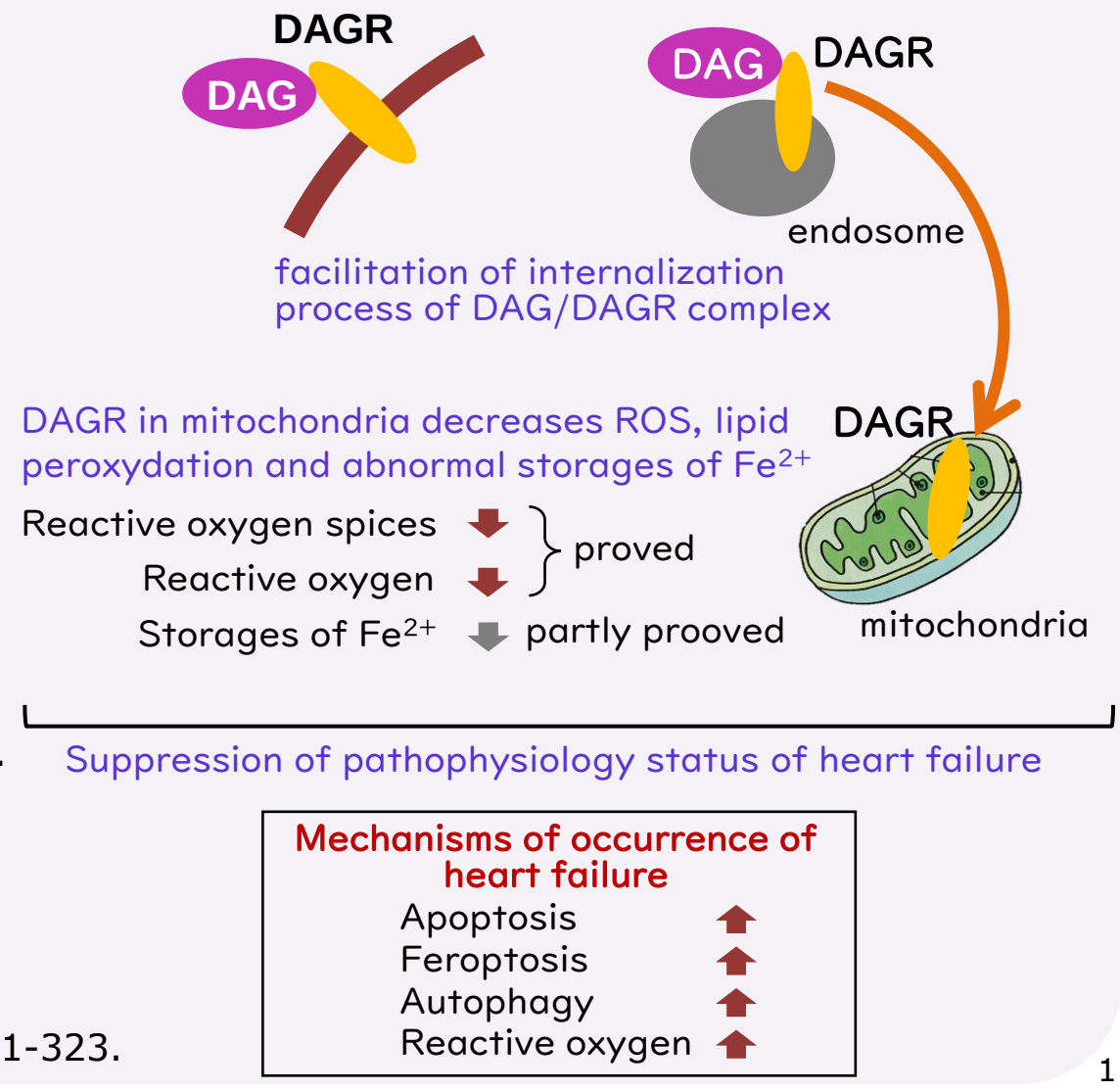
Anthracyclines are essential for cancer chemotherapy.
Persistent or late-onset cardiotoxicity develops and impedes completion of cancer treatment.
→ Long-term decline in quality of life (QOL) of cancer patients

In order to complete treatment, it is important to develop treatments that reduce such cardiotoxicity.

【Concepts】

We found that DAG, a peptide with the acyl group removed from ghrelin (an orexigenic peptide, discovered by Kojima et al. Ref. 1), ameliorated the cardiotoxicity caused by the anticancer drug DOX. At present, DAG is thought to act through intrinsic DAGR, not through ghrelin receptor signaling (Refs. 2, 3, 4).
We have identified a novel DAG receptor. In addition, DAG/DAGR signals were found to improve signals supposed to cause cardiac dysfunction (heart failure).
To date, we have utilized the DAG/DAGR assay screening system to identify novel peptides exceeding properties of endogenous DAG.

Activation of DAG/DAGR signaling suppresses cardiac insufficiency including DOX-induced cardiotoxicity by improving pathophysiological status of hearts



Mechanisms of occurrence of heart failure

Apoptosis	↑
Feroptosis	↑
Autophagy	↑
Reactive oxygen	↑

【References】

1. Kojima, Masayasu, et al. (1999) Nature 402: 656-660.
2. Baldanzi, Gianluca , et al. (2002) J Cell Biol 159: 1029-1037.
3. Yanagi, Shigehisa, et al. (2018) Cell Metab 27: 786-804.
4. Pei, Xiao M, et al. (2014) Am J Physio Endocrinol Metab 306: E311-323.

National Cancer Center (NCC) Japan / CPOT seeds

Novel Fc glycan engineering platform for development of antibody pharmaceuticals

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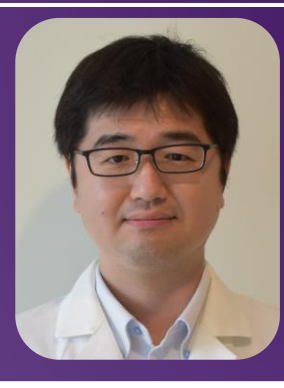
Lab Head, Developmental Therapeutics/EPOC/NCC



CPOT #21-A-13

Vision

➢ Target Product Profile

Our Fc engineering technology could control physical property, Fc-mediated effector functions, and pharmacokinetics of antibody. We could design a novel Fc structure and contribute to developing next-generation antibody pharmaceuticals.

Our Fc engineering technology is available for site-specific antibody conjugation. Thus, the technology could contribute to developing next-generation armed antibodies such as antibody-drug conjugate (ADC) and radioisotope-labeled antibody.

Under the support from the Project for Promotion of Cancer Research and Therapeutic Evolution (P-PROMOTE, AMED), we are developing our technology-based target alpha therapy in order to avoid the side effects of conventional radiotherapy.

Innovation

【Novelty】

The combination of our synthetic glycan library and an original engineering procedure results in a greater variety of Fc structures than conventional Fc engineering technologies. We could produce antibody pharmaceuticals with a novel Fc structure.

【Superiority】

1. Greater variety of Fc structures
2. Homogenous Fc structure, which strictly control functions as well as pharmacokinetics of antibodies and could reduce the risk of immunogenicity
3. Seamless progression from production of engineered antibodies to evaluation of the prototypes

Partnering

【Expected partners】

Pharmaceuticals

Biotech/Drug Discovery Service

CMO/CDMO/CRO/SMO

【Expectation】

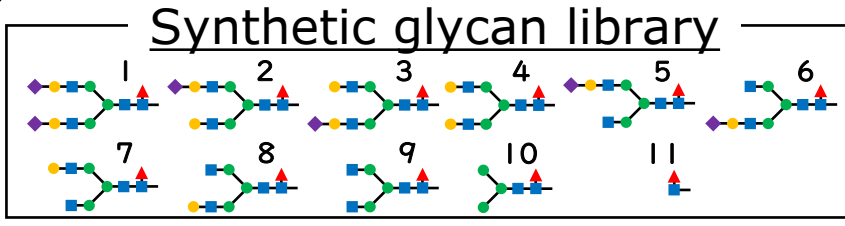
Joint development, Joint patent application

Research Outline

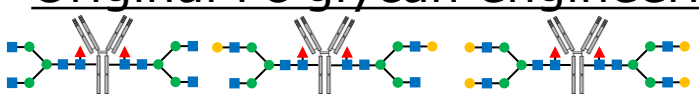
Key Words: #Antibody engineering/labeling, #Imaging

Basic technology development → Evaluation/Proof of concept → Medical application

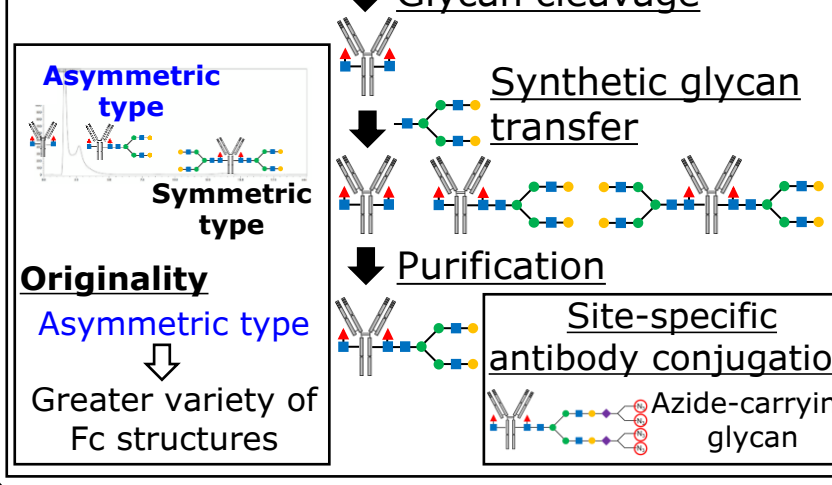
Synthetic glycan library



Original Fc glycan engineering



Glycan cleavage



Originality

Asymmetric type

⇩

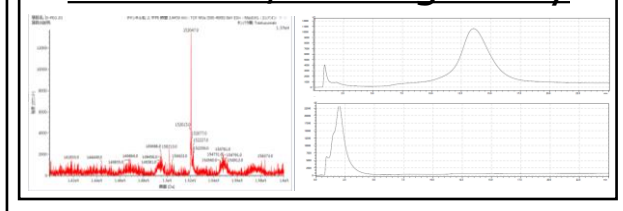
Greater variety of Fc structures

Synthetic glycan transfer

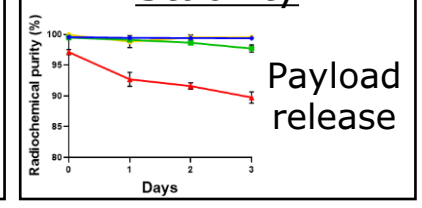
Purification

Site-specific antibody conjugation

Structure/Homogeneity



Stability



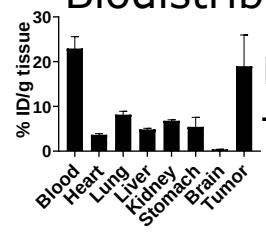
Payload release

Pharmacokinetics/Pharmacodynamics (PK/PD)

In vivo imaging

Sequential

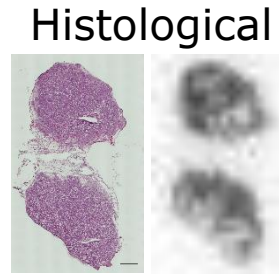
Biodistribution



Half-life

Targeting

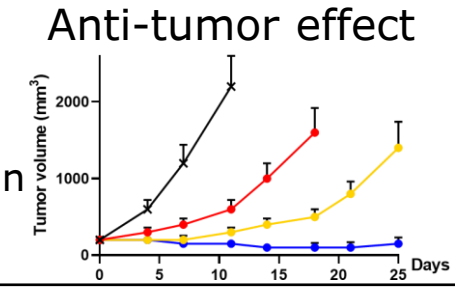
Histological evaluation



Targeting

Mode of action (MOA)

Anti-tumor effect



Controlled functions

ADCC activity
CDC activity

Controlled PK and PD

Greater tumor specificity
Lower toxicity
Controlled MOA

Antibody conjugation

Site-specific conjugation
Homogenous structure
Greater physiological property
Reduced unfavorable release

➢ References

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Takashima, Hiroki, et al. (2023) Mol Pharm 20:1156-1167.
Hiranyakorn, Methanee, et al . (2023) ACS Omega 8:16513-16518.

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