# PROGRAM BOOK

# 1st BIOLOGY AND CHEMISTRY CANCER AND AGING RESEARCH SYMPOSIUM

UNIVERSITAS INDONESIA
Veritas, Probitas, Iustitia | Ad Astra

Institute of SCIENCE TOKYO

RIKEN

BioCARES
Biology and Biochemistry Cancer and Aging Research Symposium

Depok & Jakarta, Indonesia
November 27-29th, 2024

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# WELCOME *REMARK*

by Dean of Faculty of Mathematics and Sciences, Universitas Indonesia

Dear participants and committee,

I would like to welcome you to the Biology and Chemistry Cancer and Aging Research (BioCARES) symposium. Collaboratively organized by researchers from Universitas Indonesia, Institute of Science Tokyo, and RIKEN, this symposium corresponds to the interdisciplinary need in cancer and aging research.

The aim of this symposium is to initiate the collaboration for cancer and aging research. But, it goes beyond that. I believe that this symposium will create an environment that is able to spark the researcher spirit in those who are participating. I hope that this symposium can be used as a chance to exchange knowledge, see potential collaboration, as well as a place to learn the leading research ideas from the participants.

I would like to express my gratitude to the Institute of Science Tokyo and RIKEN for the partnership, to the invited speakers from BRIN, and also to the entire event committee that has been working hard to make this event happen.

Thank you very much for your participation. I hope you can enjoy this symposium and be productive. I am looking forward to see the discussion and collaboration happen.

**Prof. Dr. Dede Djuhana**
Universitas Indonesia

# WELCOME *REMARK*

by Head of Department of Biology
FMIPA UI

Greetings,

Welcome to the Biology and Chemistry Cancer and Aging Research (BioCARES) symposium, organized collaboratively by Universitas Indonesia, Institute of Science Tokyo, and RIKEN.

As one of the global health challenges, cancer research requires collaborative interdisciplinary efforts. This symposium resembles our commitment to addressing this challenge by providing a dynamic environment for interdisciplinary collaboration for better global health.

I am confident that this workshop will produce inspiring ideas and potential collaborations for future research. By integrating our research fields, we can explore ideas and strategies to address the cancer problem through innovative and revolutionary advancements.

I would like to express my gratitude to our colleagues at the Institute of Science Tokyo and RIKEN for their partnership in initiating this event. I would also like to extend my gratitude to the invited speakers from BRIN, the national research agency of Indonesia, who will share their knowledge and experiences with us. This collaboration is proof of our commitment to address this global health problem.

For those who participate, particularly the young researchers and students participating, I hope that this workshop will broaden your knowledge and perspective. Please use this opportunity to enhance your knowledge further for future research. Share your ideas, connect with other researchers, and learn and discuss anything on this topic. Let's use this workshop to advance our knowledge and strengthen our bonds.

I look forward to the discussions and collaborations that will arise from this event.

I wish you all a productive event.

**Professor Anom Bowolaksono**
Unviersitas Indonesia

# WELCOME *REMARK*

by Head of Tanaka Lab,
Institute of Science Tokyo and
RIKEN Cluster for Pioneering
Research

Greetings,

It is with great pleasure that I welcome all of you to the "Biology and Chemistry Cancer and Aging Research (BioCARES)" workshop—a collaborative effort among Universitas Indonesia, Institute of Science Tokyo, and RIKEN.

Cancer remains one of the most pressing global health challenges, requiring innovative chemistry/biology technologies that go beyond traditional disciplinary boundaries. This workshop embodies our shared commitment to addressing this challenge by bringing together diverse perspectives and expertise. By fostering interdisciplinary collaboration, we aim to accelerate the development of advanced treatments and diagnostic methods that will benefit patients worldwide.

I am particularly excited about the potential collaborations that may arise from this workshop. The synergistic effects among Professor Anom Bowolaksono's research in Aging Biology, and Dr. Astari Dwiranti's expertise in Cancer Biology and my strategic research in Therapeutic Vivo Synthetic Chemistry, holds immense promise. By integrating our respective fields, we can explore novel therapeutic strategies that could lead to groundbreaking advancements. These interdisciplinary partnerships embody the spirit of this workshop.

I sincerely thank our colleagues at Universitas Indonesia for their invaluable partnership in making this event possible. Your enthusiasm, dedication, and warm hospitality are truly inspiring and appreciated. This collaboration is a testament to the strong bonds between our nations, and I am confident that it will bring something new ideas and strategies in future cancer research. I would also like to express my deep gratitude to the invited speakers from the National Research and Innovation Agency of Indonesia (BRIN) who will share their invaluable experiences with us.

To the young researchers and students participating, I encourage you to seize this unique opportunity across the countries. Open your eyes, share your innovative ideas, and change conventional thinking. It is such vibrant exchanges that groundbreaking ideas come up to you and lifelong professional relationships are created. Let us seize this moment to advance our scientific endeavors and strengthen our cultural and academic ties.

Once again, thank you to our Indonesian partners for your warm welcome and unwavering support. I look forward to the fruitful discussions and collaborations that will start from this workshop.

Wishing you all an inspiring and productive event.

**Professor Katsunori Tanaka**
Institute of Science Tokyo
RIKEN Cluster for Pioneering Research

# ABOUT BioCARES

**The Biology and Chemistry Cancer and Aging Research symposium (BioCARES)** is an international collaborative program that brings together researchers from the Universitas Indonesia, Institute of Science Tokyo, and RIKEN Cluster for Pioneering Research. This initiative is designed to stimulate an interdisciplinary collaboration and innovation in the fields of cancer and aging research, addressing the global health challanges.

**BioCARES** aims to create a platform for knowledge exchange, highlighting the latest scientific advances in cancer diagnostics, treatment strategies, and mechanisms. This program includes keynote presentations, oral, and poster session, which will produce a dynamic environment for discussions between researchers and academicians. We look forwards to building a strong foundation for future collaboration and scientific breakthrough through this event.

BioCARES
Biology and Biochemistry Cancer and Aging Research Symposium

# TIMELINE

| TIME | PROGRAM | |
|---|---|---|
| 08:00-08:45 | Registration | |
| 08:45-09:05 | Opening + Photo | |
| 09:05-09:20 | 6 Scientific Talk | **Keynote Lecture: Therapeutic In Vivo Synthetic Chemistry**<br>Prof. Katsunori Tanaka |
| 09:20-09.35 | | **Keynote Lecture: The Formation of DNA Adducts due to Exposure of Xenobiotics (Unsaturated Aldehydes) as Biomarkers of Cancer Risk**<br>Prof. Dr. rer. nat. Budiawan |
| 09:35-09:45 | | **Marine Natural Products for Anticancer Agents**<br>Peni Ahmadi, Ph.D. |
| 09:45-09:55 | | **Cancer Biology: Perspectives on Natural Resources as Potential Anticancer Agents, Chromosomal Dynamics, and Epigenetic Mechanisms**<br>Astari Dwiranti, Ph.D. |
| 09:55-10:05 | | **Cancer On-Site Synthesis of Active β-Carboline Derivative Using Intramolecular Azaelectrocyclization**<br>Kazuki Terashima |
| 10:05-10:15 | | **Utilization of [3+2] Cycloaddition with Endogenous Acrolein for Cancer Treatment in Patient-Derived Xenograft Models**<br>Yuria Takahashi |
| 10:15-10:30 | Coffee Break | |
| 10:30-10:40 | 6 Scientific Talk | **Targeted Therapy for *KRAS*-mutant Cancer using Glycosylated Artificial Metalloenzymes via Therapeutic *In Vivo* Synthetic Chemistry**<br>Tsung-Che Chang, Ph.D. |
| 10:40-10:50 | | **Evaluation of Insulin-Transferrin-Selenium (ITS) Supplement as Serum Replacement In Serum-Free Circulating Tumor Cell Culture**<br>Muhammad Altaf Aaron Zakaria |
| 10:50-11:00 | | **Exploring Lewis-Acid Catalyzed Reactions in Blood for *In Vivo* Therapeutic Applications**<br>Ren Kumakura |

| TIME | PROGRAM | |
|---|---|---|
| 11:00-11:10 | 6 Scientific Talk | **Effects of *Simmondsia chinensis* (Link) Schneider Seed Oil towards the Viability and Ultrastructure of Cancer Cells A549, MCF-7, and MDA-MB**<br>Vinka Valencia Liman |
| 11:10-11:20 | | **Anticancer Strategy Using Alcohol Metabolites via Therapeutic *In Vivo* Synthetic Chemistry**<br>Koichi Ishida |
| 11:20-11:30 | | **Isolation and Characterization of Circulating Tumor Cells Expressing Plastin-3 (PLS3) Using Density Gradient and Erythrolysis Methods**<br>Annisa Rahmani Putri |
| 11:30-12:30 | Poster Session | |
| 12:30-14:00 | Lunch | |
| 14:00-14:10 | 7 Scientific Talk | **Biofunctional Chemistry and Reactivity of Biogenic Metabolites for Cancer Diagnosis and Therapy**<br>Ambara R. Pradipta, Ph.D. |
| 14:10-14:20 | | **Extrachromosomal DNA in Breast Cancer Cell Lines: Detection and Characterization**<br>Shadira Anindieta Irdianto |
| 14:20-14:30 | | **Targeted Radioisotope Therapy via [3+2] Cycloaddition with Cancer Metabolites**<br>Yudai Ode |
| 14:30-14:40 | | **In vitro screening of several Indonesian herb extracts against Dengue virus serotypes 2 and 4**<br>Sabar Pambudi, Ph.D. |
| 14:40-14:50 | | **Synthesis of Functional Polymers in Cancer Cells via Uncatalyzed [4+4] Cycloaddition for Cancer-Selective Detection**<br>Shinji Kawaguchi |
| 14:50-15:00 | | **Caffeine-Induced Modulation of Cellular Death and Telomerase Activity in Breast Cancer Cell Lines**<br>Qanita Hana Amira |
| 15:00-15:10 | | **Amidation with Polyamines from Cancer Cells for In Vivo Drug Synthesis**<br>Atsuhiro Matsuura |
| 15:10-15:30 | Coffee Break | |

| TIME | PROGRAM | |
|---|---|---|
| 15:30-15:40 | 7 Scientific Talk | **Targeted Drug Synthesis in Cancer Cells via Palladium-catalyzed Reaction with Endogenous CO**<br>Masayuki Kawai |
| 15:40-15:50 | | **Effects of Hemin Combination on Aminolevulinic Mediated Photodynamic Therapy (ALA-PDT) in A549 Lung Cancer Cell Line**<br>Rahma Wirdatul Umami |
| 15:50-16:00 | | **Gold-Catalyzed Synthesis of Fluorescent Dyes Derived from Cancer Metabolites**<br>Shunya Ohara |
| 16:00-16:10 | | **Cloning and Expression of SCAMP3 in DH10Bac as An Inducer for anti-SCAMP3 Monoclonal Antibody**<br>Selly Setianti Rajagukguk |
| 16:10-16:20 | | **Therapeutic In Vivo Synthetic Chemistry Using a Novel Anticancer Compound Derived from Bracken Poison**<br>Tatsuya Kobayashi |
| 16:20-16:30 | | **Resourcing Mouse Blood Albumin as a Biocompatible Artificial Metalloenzyme for Colorectal Cancer Therapy**<br>Kyosuke Imai |
| 16:30-16:45 | | **Keynote Lecture: Natural Solutions to Alleviate Signs of Dermal Aging**<br>Prof. Anom Bowolaksono |
| 16:45-17:00 | Closing remark | |

## Scientific Poster List

| | |
|---|---|
| 1 | **Effect of Caffeine on Cell Viability and hTERT Gene Expression in A549 Lung Cancer Cells**<br>Yasmin Verena Jerissia Murtagh |
| 2 | **Roles of Butyrate in Inflammatory Orbital Fibroblast from Graves' Ophthalmopathy Patients**<br>Fadhil Rafi Azkarnaen |
| 3 | **Effect of Inhibitor BIX01294 in Inhibiting EHMT1 Gene Expression in A549 Lung Cancer Cells**<br>Azka Alfathi Madani |

## Scientific Poster List

| | |
|---|---|
| 4 | **Effect of Simmondsia chinensis (Link) Seeds Oil towards the Viability, Apoptosis, and Ultrastructure of Breast Cancer MDA-MB-231**<br>Frieska Amelia Widya Ananda |
| 5 | **Jojoba (Simmondsia chinensis (Link) Schneider) Seed Oil Effect on the Viability and Ultrastructure of MCF-7 Breast Cancer Cell**<br>Qurrothul Dwi AIni |
| 6 | **Epidermal and Fibroblast Growth Factor Affect in vitro Culture of Circulating Tumor Cell from Colorectal Cancer in a Concentration Dependent Manner**<br>Rafli Maulana Muhammad |
| 7 | **Autophagy-Mediated Protein Degradation in Cancer Cells Induced by Acrolein-Azide [3+2] Cycloaddition**<br>Kana Hasegawa |
| 8 | **Therapeutic In Vivo Synthetic Chemistry with Gold Artificial Metalloenzymes for Brain Cancer Treatment**<br>Moeri Hara |
| 9 | **Selective Labeling and Functional Analysis of Cancer Cells using Artificial Metalloenzymes**<br>Sawa Inukai |
| 10 | **Treatment of Tumor Bleeding by Therapeutic In Vivo Ring-Opening Metathesis Polymerization**<br>Yoshito Nakada |
| 11 | **Utilization of Tailor-Made Synthetic Glycoalbumins for Cancer Treatment**<br>Akito Nunome |
| 12 | **Exploiting the Diels-Alder Reaction with Endogenous Acrolein for Cancer Treatment**<br>Yuki Masaki |
| 13 | **Selective Activation of PROTACs in Cancer Cells via Metathesis Reaction using Artificial Metalloenzymes**<br>Yuta Shimura |
| 14 | **Synthesis and Enzymatic Degradation of D-Arabinan Fragments from Anticancer Immunostimulating Mycobacterial Cell Wall Skeleton**<br>Akhiro Ishiwata |
| 15 | **Synthesis of Tricyclic Diterpenoid Using Artificial Metalloenzymes**<br>Riichi Hashimoto |
| 16 | **Cancer Treatment PDO and PDX Models Using Therapeutic *In Vivo* Synthetic Chemistry**<br>Akiko Nakamura |

# Therapeutic *In Vivo* Synthetic Chemistry

Katsunori Tanaka

Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Institute of Science Tokyo, Japan.
Biofunctional Synthetic Chemistry Laboratory, RIKEN Cluster for Pioneering Research, Japan

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The long-term goal of our research is to develop the working tools and methodologies that will form the foundation of "Therapeutic *In Vivo* Synthetic Chemistry". The main benefit of this approach is that synthetic transformations can be directly performed at target regions within the body to generate molecules that elicit localized biological effects. This method should largely circumvent off-target binding and instability issues associated with current drug administration techniques. In these years, we have engaged this topic through two different approaches. The first is through the usage of glycosylated artificial metalloenzymes, where the primary aim is to exploit the chemoselectivity of embedded, non-natural transition metal catalysts for the synthesis/release of bioactive molecules. The second approach is rather centered on discovering chemical probes with novel and selective reactivity to biological metabolites naturally overexpressed in cancer cells. Once developed, the objective is then to adapt them for synthesizing diagnostic probes or anticancer drugs. A part of our strategies has already met with successful outcome in clinical trials and could be applied to pharmaceutical fields and hospitals. Overview and future prospect will be discussed.

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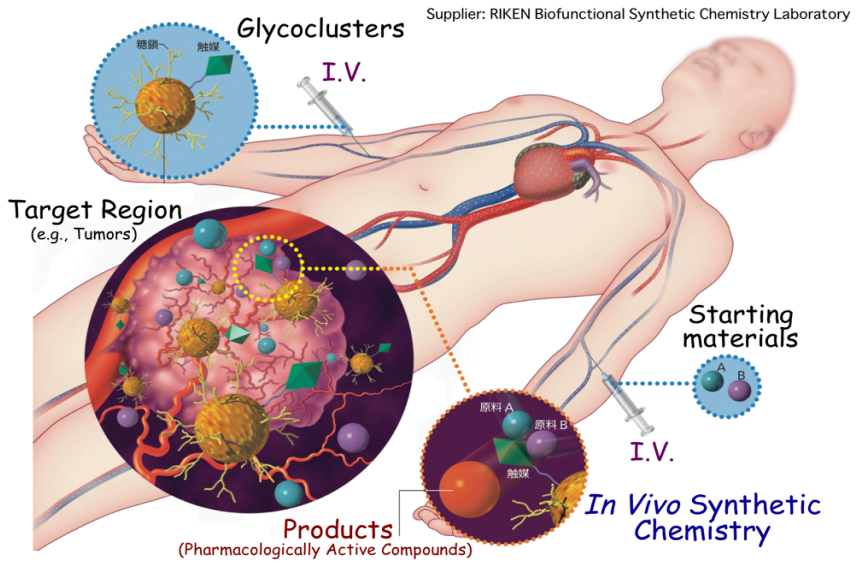
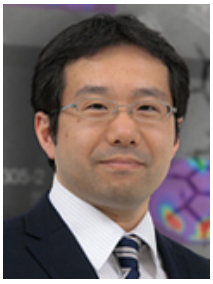
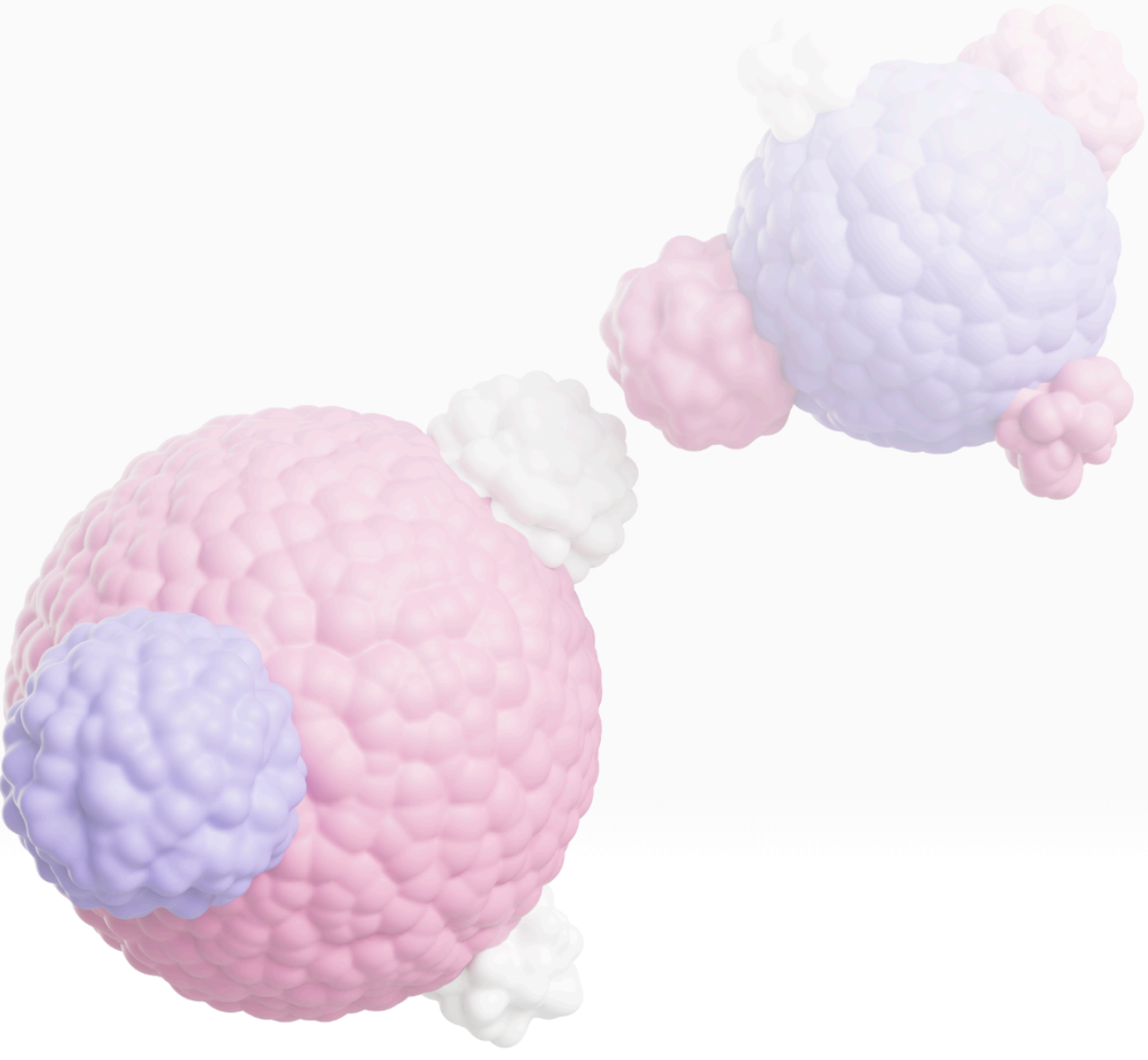




**Prof. Katsunori Tanaka**
*Professor of Institute of Science Tokyo and Researcher at RIKEN Cluster for Pioneering Research*

Katsunori Tanaka achieved his Ph.D. in Chemistry from Kwansei Gakuin University. He then became an assistant professor at Osaka University. Now, He holds concurrent roles as a Professor at the Institute of Science Tokyo and as a Chief Scientist at the RIKEN institute. His research interests include organic synthesis, molecular imaging, in vivo synthesis, and natural products.



# Chemicals in Carcinogenic (Genotoxicity) studies: DNA Adducts formation due to exposure to Xenobiotics ( α, β-Unsaturated Aldehydes) as Cancer Risk Biomarker

Budiawan

Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, 16424, Indonesia

Chemicals are elements or compounds, both natural and synthetic, that play an important role in various aspects of life, such as foods, energy, batteries, industry, health, cosmetics, and the environment. On the one hand, chemicals offer enormous benefits in improving the quality of life, but on the other hand, there is a risk of harmful properties inherent in chemicals such as the increase in cancer from year to year caused by exposure to certain chemicals. Through chemical toxicology (genotoxic) studies, namely DNA-adduct formation, the long-term impact of certain substances such as carcinogenic/mutagenic chemicals (alpha, beta-unsaturated aldehyde compounds, polyaromatic hydrocarbons, and other chemicals) that risk causing cancer or genetic damage can be known and controlled to minimize risk.

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**Prof. Dr. rer. nat. Budiawan**
*Professor*
*Universitas Indonesia*

Prof. Dr. rer. nat. Budiawan is a Professor at the Department of Chemistry, Universitas Indonesia. He earned his Ph.D. from the University of Würzburg. His research focus is on toxicology, chemistry, and environmental ecology. He earned his professor title in 2023.

# Marine Natural Products to Cancer Therapy

Peni Ahmadi
Research Center for Vaccine and Drugs, Research Organization for Health, National Research and Innovation Agency of the Republic of Indonesia (BRIN), Jl. Jakarta-Bogor, Km. 46, Cibinong, Bogor, West Java, 16911, Indonesia.

Latrunculin A (LatA) has been reported to elicit an excellent strong activity against cancerous cells. LatA accelerates actin filament depolymerization and has been used as a research tool in cell biology and molecular studies to investigate the roles of actin in various cellular processes. However, Lat A has not even entered a preclinical trial for an anticancer drug. Previously, our group investigated the anticancer activity of LatA against cervical cancer (HeLa), lung cancer (A459), breast cancer (MCF-7), and kidney normal cells for control (Hek293). The $IC_{50}$ values of LatA against HeLa, A549, MCF-7, and Hek293 are 213.5, 252.2, 16.13, and 200.000 nM, respectively. It is indicated that LatA is confirmed to have a potential used as an anticancer drug which is selectively active against cancerous cells and relatively safe towards normal cells. These magnificent results of LatA being very active at a tiny concentration brought us to come up with a new idea and strategy to use LatA as a drug to treat cancer stemness and metastasis in addition to treating primary cancer. Hence, we would like to investigate the potential use of LatA as an anticancer drug for treating primary cancer, cancer cell stemness, and m main project on drug discovery and de

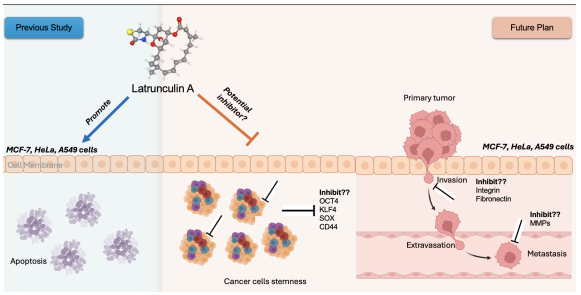



Figure 1. The anticipated mechanisms of action of LatA against cancerous cells.

**Peni Ahmadi**
*Researcher*
*National Research and Innovation Agency of the Republic of Indonesia*

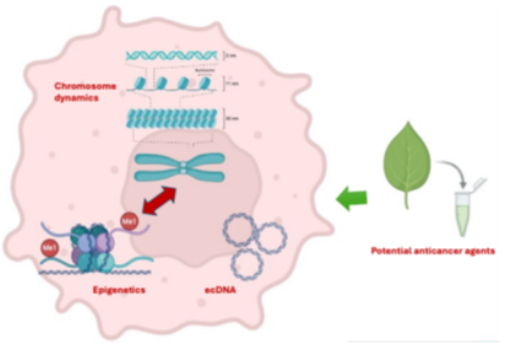
Peni Ahmadi earned her Ph.D. in Marine Environmental Sciences, University of the Ryukyus in 2017. In the same year, she got a postdoc position in RIKEN, Japan, under the supervision of Prof. Katsunori Tanaka. In 2021, she has officially joined National Research and Innovation Agency of the Republic of Indonesia and continued her research in the field of marine natural products and their application for cancer therapy.

# Cancer Biology: Perspectives on Natural Resources as Potential Anticancer Agents, Chromosomal Dynamics, and Epigenetic Mechanisms

Astari Dwiranti

Integrated Cellular and Molecular Biology (ICEMBIO) Laboratory, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, 16424, Indonesia
E-mail: astari.dwiranti@sci.ui.ac.id

Cancer biology research seeks to answer a crucial question: What differentiates normal cells from cancerous ones? Understanding these distinctions is key to unraveling the mechanisms of cancer initiation, progression, and metastasis. This talk explores critical contributors to cancer biology, including chromosome dynamics and epigenetic modifications. The reversible nature of chromosomal structure influenced and its correlation with the emerging phenomenon of extrachromosomal DNA in cancer research will be discussed. Furthermore, advancing cancer biology knowledge also enables the exploration of potential anticancer agents. Natural compounds have emerged as promising candidates for cancer therapy, offering strategies to prevent, inhibit, and treat the disease. Indonesia, with its rich biodiversity, host approximately 7,000 medicinal plant species. Among them, *Spatolobus littoralis* Hassk. and *Chrysopogon zizanioides* (L.) Roberty are known to contain bioactive compounds such as flavonoids, alkaloids, steroids, and vetiverol. Despite this, their anticancer potential remains underexplored. This study evaluates these plant extracts' effects on cancer cell viability and membrane ultrastructure. Optimal concentrations for reducing cancer cell viability were identified using various approaches, and scanning electron microscopy revealed potential mechanisms of action at the cellular level. This presentation highlights our findings and emphasizes the opportunities and challenges in leveraging Indonesia's biodiversity for cancer research. Our work underlines the importance of integrating molecular insights with natural product exploration to advance cancer therapy development.

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**Astari Dwiranti**
*Associate Professor*
*Universitas Indonesia*

Astari Dwiranti, M.Eng., Ph.D. is an Associate Professor at the Department of Biology, Universitas Indonesia. With a Ph.D. and M.Eng. in Biotechnology from Osaka University, her work spans cell biology, chromosome studies, and cancer biology research.

# Cancer On-Site Synthesis of Active β-Carboline Derivative Using Intramolecular Azaelectrocyclization

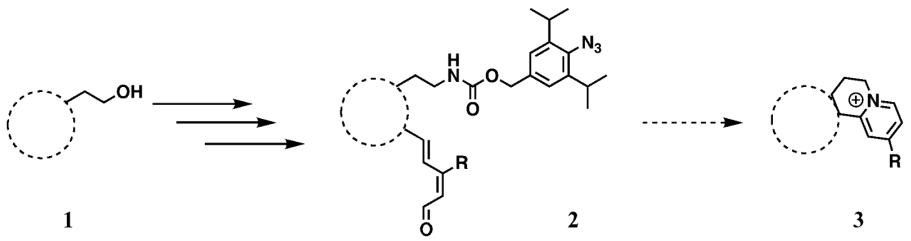
Kazuki Terashima,[1] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

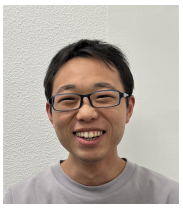
In our previous research, we observed that acrolein is excessively produced in cancer cells but is negligible in healthy cells. Furthermore, we have successfully developed a prodrug strategy that selectively releases the anticancer drug only in the cancerous tissue through a reaction with endogenous acrolein in a xenograft mouse model.

Herein, we have developed a novel method to synthesize a zwitterionic bicyclic compound **3** from a precursor compound **2**. The deprotection of the primary amine of compound **2** through a reaction with endogenous acrolein in cancer cells leads to an intramolecular 6π-azaelectrocyclization, resulting in the partial structure of a β-carboline natural product.

We aim to apply this chemistry to the in situ natural product synthesis within cancer cells by initiating a reaction with endogenous acrolein. We will discuss the synthesis of precursor compound **2** from commercially available compound **1** and the conversion of precursor **2** to the target compound **3**. Additionally, we discuss the structure-activity relationship of the derivatives against cancer cells.

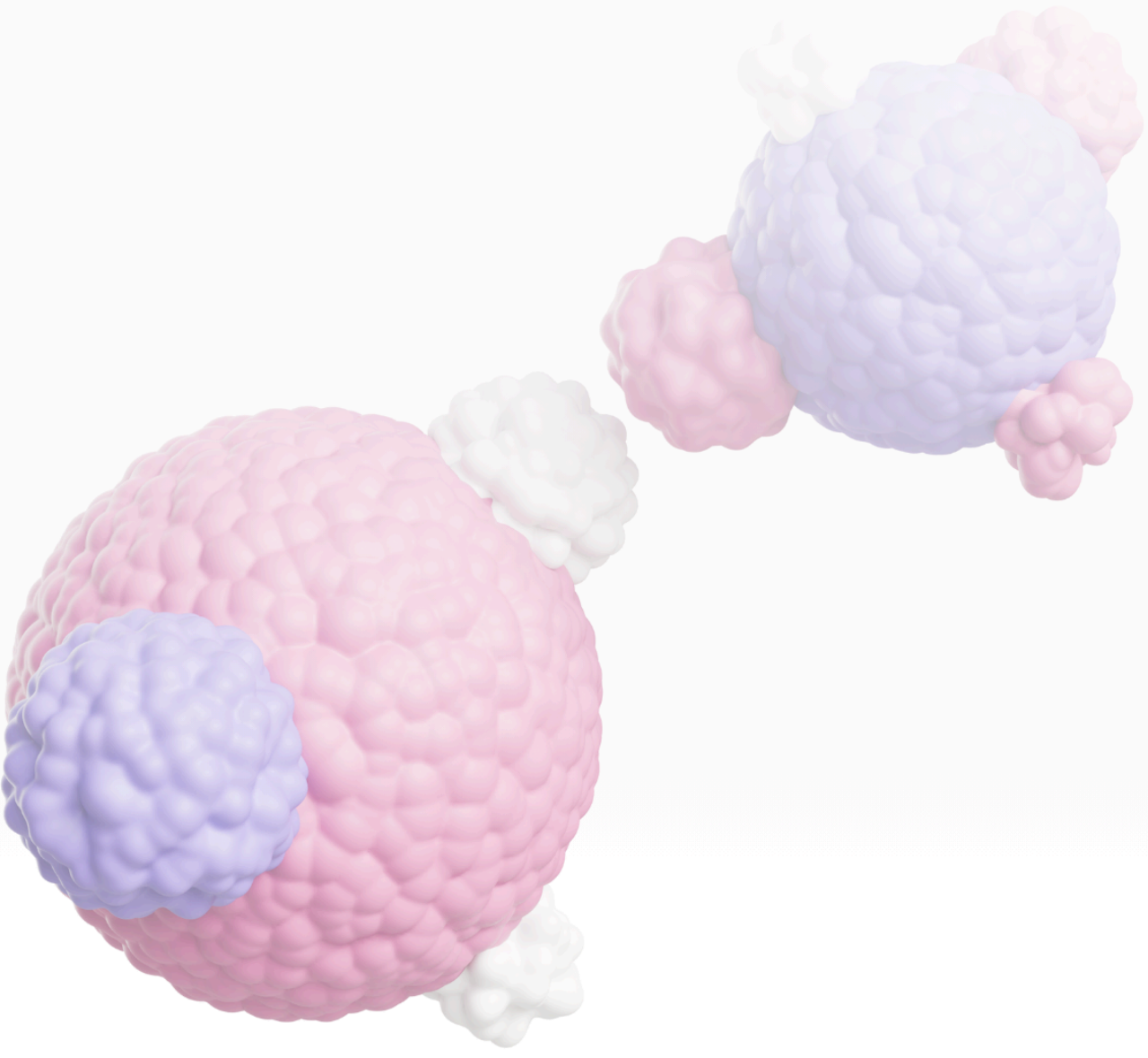



1. T. Tanei, A. R. Pradipta, K. Morimoto, M. Fujii, M. Arata, A. Ito, M. Yoshida, E. Saigitbatalova, A. Kurbangalieva, J. -I. Ikeda, E. Morii, S. Noguchi and K. Tanaka, *Adv. Sci.* **2019**, *27*, 2228-2234.
2. A. R. Pradipta, P. Ahmadi, K. Terashima, K. Muguruma, M. Fujii, T. Ichimo, S. Maeda and K. Tanaka, *Chem. Sci.* **2021**, *12*, 5438-5449.



**Kazuki Terashima**
*Doctoral Student, Tokyo Institute of Technology*

Kazuki Terashima (寺島 一輝). Tokyo Institute of Technology. Doctoral Course, 2nd year. Research Field: In Vivo Synthetic Chemistry.



# Utilization of [3+2] Cycloaddition with Endogenous Acrolein for Cancer Treatment in Patient-Derived Xenograft Models

Yuria Takahashi,[1] Kazuki Terashima,[1] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

In the context of cancer treatment, it is crucial to minimize the adverse effects of anticancer medications. One emerging approach to tackle this challenge is the chemistry-based method. We have previously developed a prodrug strategy using [3+2] cycloaddition of endogenous acrolein, which is overexpressed in various cancers (*Chem. Sci*. **2021**, *12*, 5438.).

In our latest study, we elucidated the mechanism and assessed the effectiveness of our prodrug in patient-derived xenograft (PDX) models, employing a prodrug of doxorubicin (DOX), a drug commonly used in cancer treatment but limited in dosage due to its side effects (Figure 1). The DOX-prodrug exhibited potent anticancer effects without side effects even at high doses against A549 cell xenograft–bearing nude mice. Pharmacokinetic and serum protein binding studies confirmed that the DOX-prodrug improved the albumin binding property, thereby increasing circulatory residence and serum stability compared to the parent DOX. This stabilized prodrug can be activated gradually at the cancer site by reacting with endogenous acrolein, releasing the required amount of the drug molecule. Importantly, the DOX-prodrug demonstrated selective anticancer effects against PDX models of lung, colorectal, gastric, and breast cancers. Our in vivo chemical strategy may be suitable for future clinical trials.

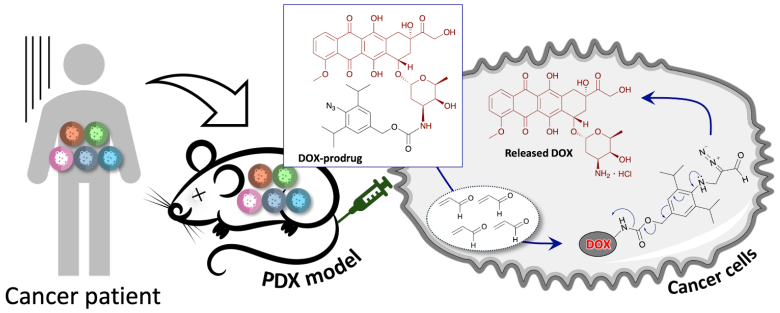
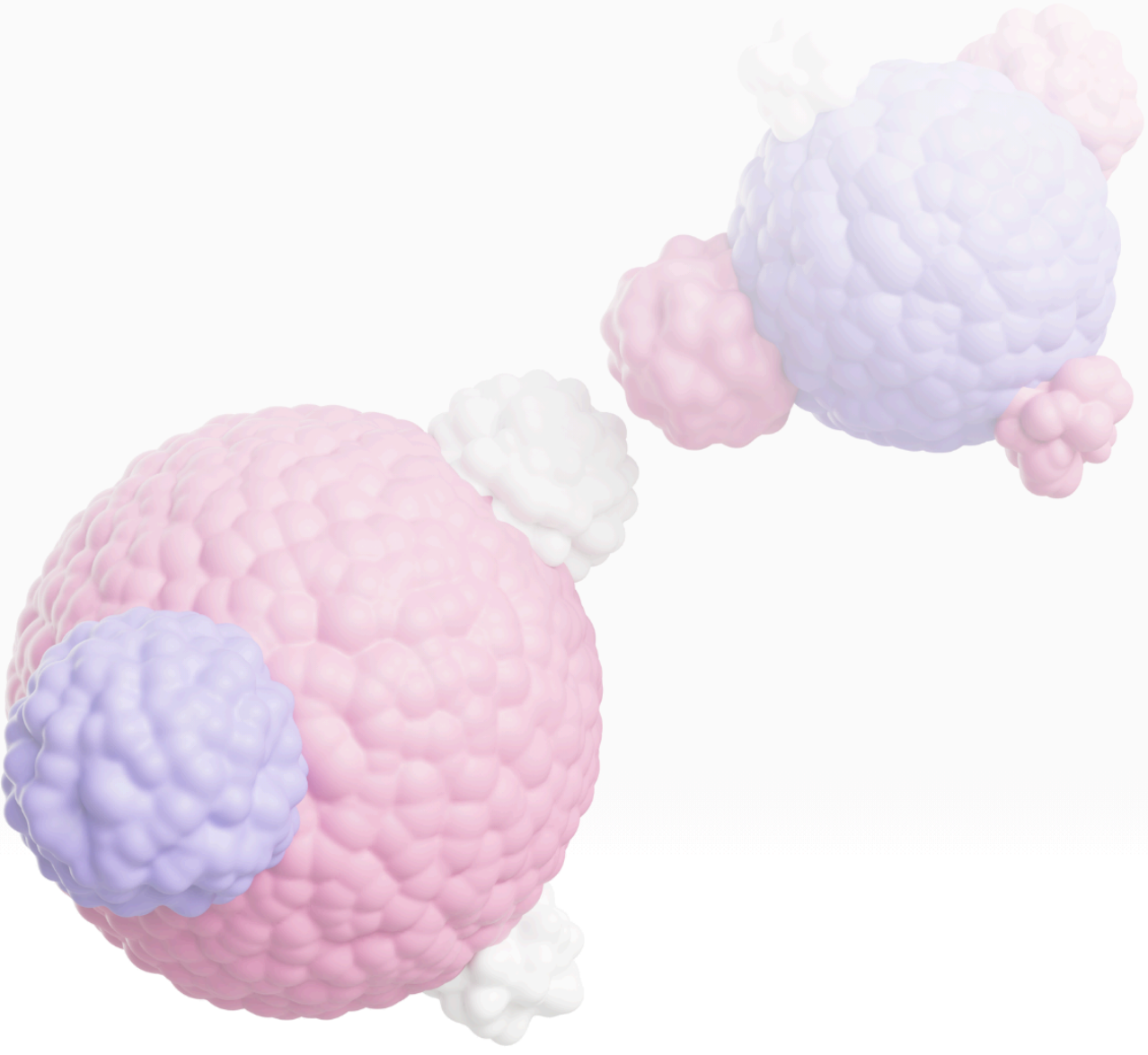



**Figure 1.** Antitumor effects of DOX-prodrug in PDX models

**Yuria Takahashi**
*Master Student,*
*Tokyo Institute of Technology*

Yuria Takahashi (髙橋 ゆりあ) completed her bachelor studies in the Department of Chemical Science and Engineering, Tokyo Institute of Technology in 2023. She is currently 2nd Year Student of Master Course. Her expertise lies in organic chemistry, bioorthogonal chemistry, and *in vivo* synthesis. Her research focuses on developing prodrug utilizing [3+2] cycloaddition with endogenous acrolein. In her free time, she enjoys reading books.



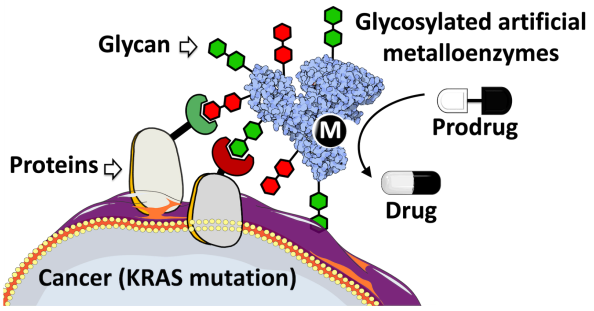
# Targeted therapy for *KRAS*-mutant cancer using glycosylated artificial metalloenzymes via therapeutic *in vivo* synthetic chemistry

Tsung-Che Chang,[1] Akiko Nakamura,[1] Hiromasa Yoshioka,[1] Yuriko Kusakari,[1] Katsunori Tanaka[1,2]

[1]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan
[2]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan

*KRAS* mutations are found in approximately 25% of cancers, and they are associated with aggressive tumor growth and shorter survival. Unfortunately, despite 40 years of proprietary drug effects, there are still no effective strategies targeting *KRAS* mutants, except for Sotorasib, which has just been approved to target the mutated *KRAS* subtype *KRAS*(G12C) with a covalent inhibition. Glycan recognition with proteins is one of the primary components that causes cell-to-cell contacts. Because most cancer cells, compared to healthy cells, alter glycosylation patterns to react with various proteins, this could be a possible targeting method for *KRAS* mutant malignancies.

Here we have identified a kind of glycoalbumin that can specifically target a *KRAS* mutant patient-derived tumor organoid (PDO). Furthermore, the direct synthesis of drugs at disease sites in vivo, named as "*Therapeutic In Vivo Synthetic Chemistry*" enables drugs to treat diseases without causing side effects in healthy tissues. Adapting the targeting glycoalbumin to become a glycosylated artificial metalloenzyme (GArM)[1], in vitro and in vivo results showed that our "*Therapeutic In Vivo Synthetic Chemistry*" could induce a significant inhibition of cancer cells growth in PDO and patient-derived xenograft (PDX) model.




*References*:

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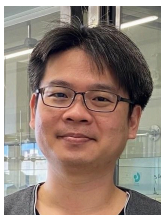
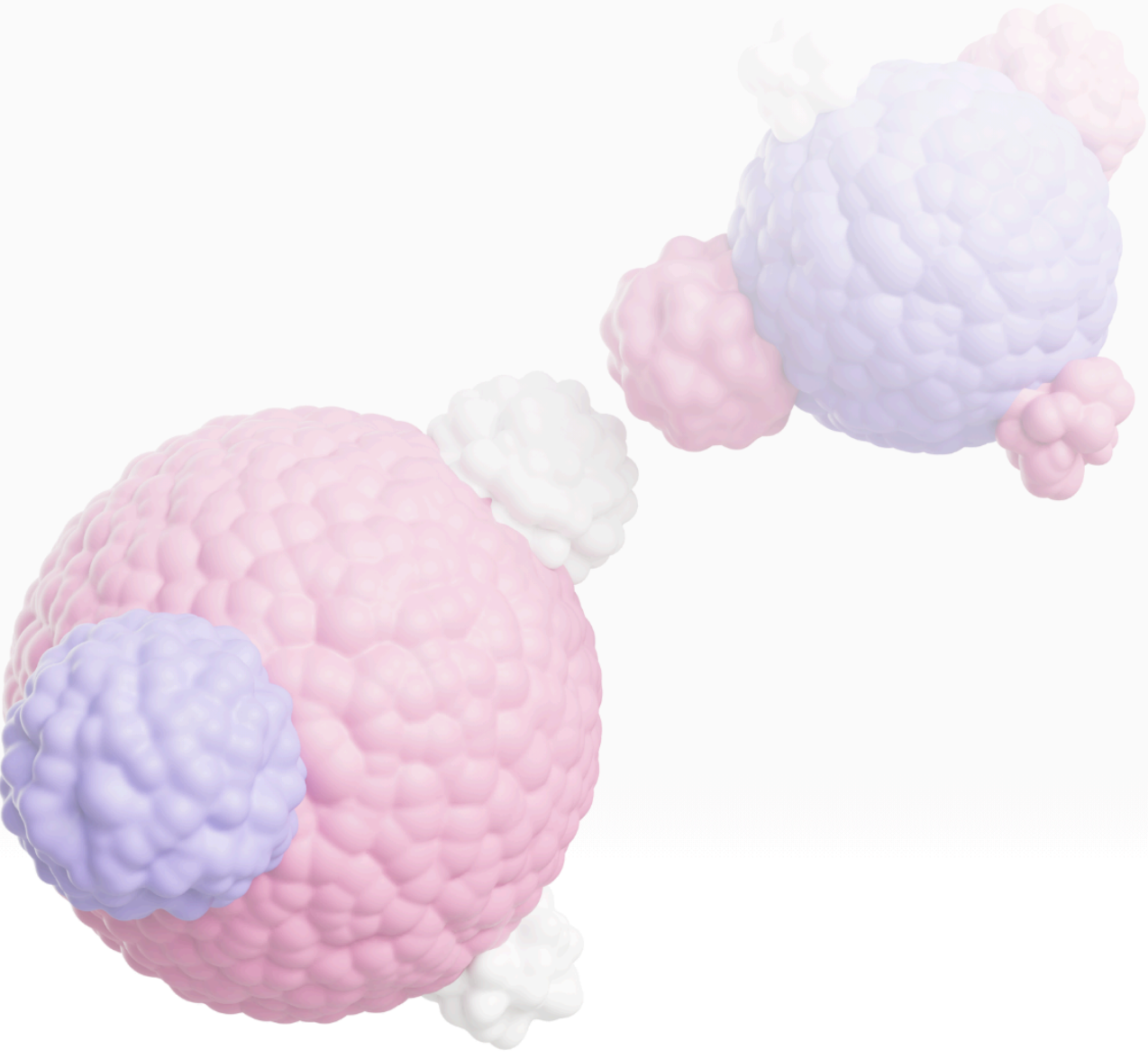


**Tsung-Che Chang**
*Research Scientist, RIKEN Cluster for Pioneering Research*

Tsung-Che Chang earned his Ph.D. in chemistry from National Tsing-Hua University in 2012. Following a one-year postdoctoral research position at Taiwan's National Health Research Institutes, he served as a JSPS postdoctoral fellow from 2013 to 2015 and as a special appointment assistant professor from 2015 to 2018 at Osaka University. After that, he undertook another postdoctoral position from 2018 to 2023 at RIKEN and was a special appointment assistant professor from 2023 to 2024 at Tokyo Institute of Technology. Since April 2024, he has been working in his current position. His research interests include carbohydrate chemistry, biocatalysis, and therapeutic in vivo synthetic chemistry.



# Evaluation of Insulin-Transferrin-Selenium (ITS) Supplement as Serum Replacement In Serum-Free Circulating Tumor Cell Culture

Muhammad Altaf A. Zakaria[1], Anom Bowolaksono[1], Astari Dwiranti[1*]

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Circulating tumor cells (CTCs) play a critical role in cancer metastasis and hold potential for diagnosis, prognosis, and therapy. Effective CTC culture is essential for advancing these applications but remains challenging. While serum-free media offer consistency for studying cell physiology and signaling, supplementation is necessary to support CTC growth[1]. This study investigates the effects of fetal bovine serum (FBS) and insulin-transferrin-selenium (ITS) supplementation at 1X and 10X concentrations on CTC cultures from erythrolysis-isolated cells. Cultures were maintained for 18 days, with cell viability assessed over six days and morphological features evaluated. Unlike FBS-supplemented medium, serum-free media supplemented with ITS did not induce spheroid formation. On day 18, CTCs' survival was verified using CK20 and PLS3 immunofluorescence markers. Results showed that 10X ITS significantly enhanced the growth of colorectal cancer CTCs, evidenced by larger cell diameters compared to 1X ITS and 10% FBS. These findings highlight the critical role of ITS in serum-free CTC culture and its potential to optimize growth without promoting spheroid formation, offering valuable insights for future cancer research.

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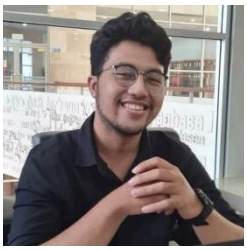

**M. Altaf A. Zakaria**
*Undergraduate Student, Universitas Indonesia*

Muhammad **Altaf** Aaron Zakaria recently graduated with a bachelor's degree in Biology, where he developed a strong interest in endocrinology, nutrition, and physiological pathology research. His undergraduate thesis focused on optimizing *in vitro* circulating tumor cell (CTC) expansion mediums, showcasing his dedication to innovative scientific exploration. He aspires to further his academic journey by specializing in diabetes research, aiming to contribute to advancements in this critical field. Beyond his academic pursuits, Altaf is passionate about education advocacy, actively supporting initiatives to improve primary to senior high school education in Indonesia.

# Exploring Lewis-Acid Catalyzed Reaction in Blood for *In Vivo* Therapeutic Application

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[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
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Lewis acid catalysts have been wildly used to catalyze various organic transformations; however, they cannot work in vivo because of deactivation by biomolecules. Previously, we have found that incorporating metal catalysts into the hydrophobic pockets of albumin to form artificial metalloenzymes (ArMs) can protect their reactivity in vivo.[1] In this study, we successfully anchored a kind of Lewis acid into albumin to create a Lewis acid-based ArM. We demonstrated that the Lewis acid-based ArM was able to catalyze the Mannich reaction in blood solution (as shown in Fig. 1). Moreover, we discovered that modifying the albumin surface with specific glycans can induce selective accumulation of them in cancer sites in vivo.[2] Together with cancer-targeting glycans, we will utilize the in vivo Mannich reaction to synthesize anticancer compounds for cancer treatment to avoid unwanted side effects. More information on this topic will be presented in the symposium.

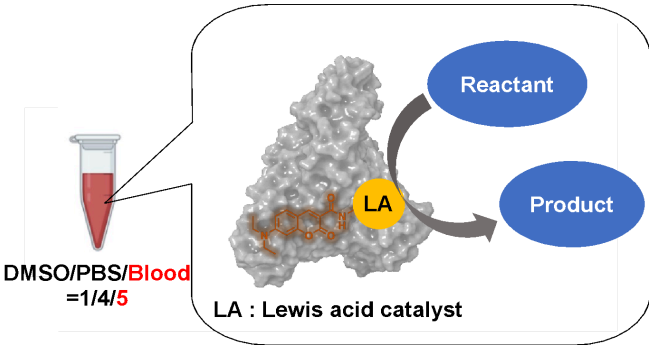


**Fig. 1** Lewis acid catalyst reaction in blood

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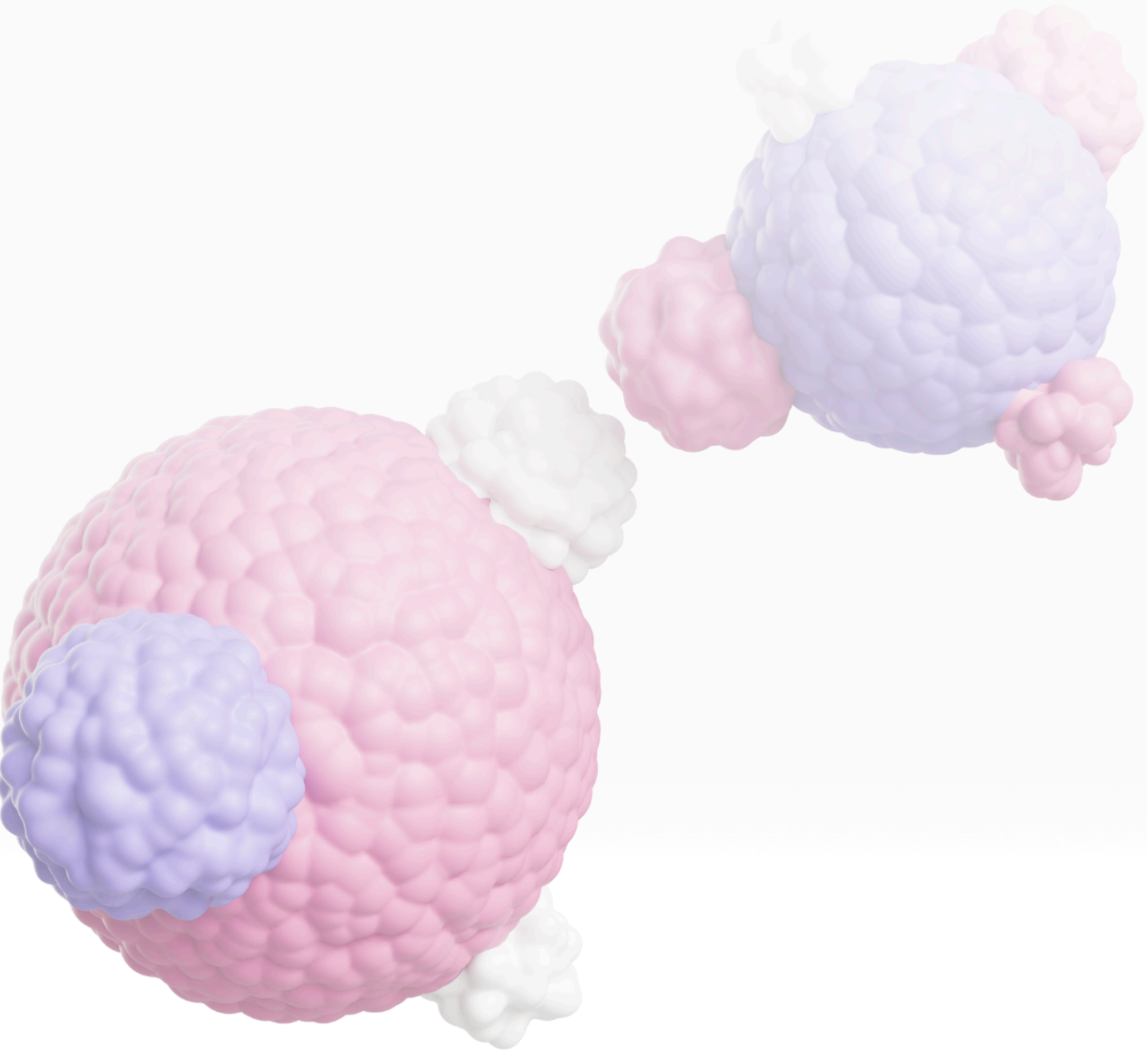
**Ren Kumakura**
*Doctoral Student, Tokyo Institute of Technology*

Ren Kumakura completed his Master studies in the Department of Chemical Science and Engineering at Tokyo Institute of Technology in 2022. His expertise lies in bioorganic chemistry, organic synthesis chemistry, and natural product chemistry. In his holiday, he enjoys watching soccer and table tennis.



# Effects of *Simmondsia chinensis* (Link) Schneider Seed Oil on the Viability and Ultrastructure of A549 Lung Cancer Cells

Vinka Valencia Liman[1], Shadira Anindieta Irdianto[1], Fadhillah[1], Saifudin[1], Anom Bowolaksono[1], Astari Dwiranti[1*]

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Lung cancer remains the cancer with the highest morbidity and mortality worldwide, both in men and women.[1,2] The use of chemotherapy in lung cancer therapy may lead to cancer cell resistance against chemotherapeutic agents as well as serious side effects. Therefore, the exploration of natural anticancer agents has become one of the main focus in current cancer research.[3] Jojoba (*Simmondsia chinensis* (Link) Schneider) is one of the plants that is known for its unique seed wax ester oil and has various potentials, one of which is anticancer.[4] Jojoba seed oil and extracts have been reported to exert cytotoxic effects on the viability of HCT-116 colorectal cancer cells, MCF-7 breast cancer cells, and MV-3 melanoma cells in a recent study using the MTT assay method by Al-Qizwini et al. (2014).[5] However, the effect of jojoba seed oil on the viability and ultrastructure of A549 lung cancer cells has not been previously determined. This study aims to determine the effect of various concentrations of jojoba seed oil (50, 100, 200, 300, 400, and 500 µg/mL) on A549 cell viability by trypan blue method and ultrastructure by scanning electron microscopy method. The test results and statistical analysis proved that jojoba seed oil with concentrations of 100, 200, 300, 400, and 500 µg/mL had a significant effect on reducing A549 cell viability. The jojoba seed oil concentration of 300 µg/mL can also cause ultrastructural changes on A549 cells. We will provide more details on the findings of this study and the potential future follow-up studies in the symposium.

*References*: (1) A. Cyzlkowska, B. Rogalewicz, M. Szczesio, A. Raducka, K. Gobis, P. Szymanski, K. Czarnecka, B. C. Camargo, J. Szczytko, A. Babich, S. Dubkov, P. Lazarenko, *International Journal of Molecular Sciences*. **2022**, *23*, 2980; (2) L. Korrodi-Gregório, V. Soto-Cerrato, R. Vitorino, M. Fardilha, R. Pérez-Tomás, *PLoS ONE*. **2016**, *11*, 11; (3) A. Hanif, A. H. Ibrahim, S. Ismail, S. S. Al-Rawi, J. N. Ahmad, M. Hameed, G. Mustufa, S. Tanwir, *Molecules*. **2023**, *28*, 2812; (4) A. P. Siahaan, E. Rohaeti, A. M. Muddathir, I. Batubara, *Biosantifika: Journal of Biology & Biology Education*. **2020**, *12*, 3; (5) H. Al-Qizwini, E. Al-Khateeb, N. M. Mhaidat, A. Saleem, *European Scientific Journal*. **2014**, *10*, 24

**Vinka Valencia Liman**
*Student, Universitas Indonesia*

Vinka Valencia Liman finished her degree as Bachelor of Science from the Department of Biology Universitas Indonesia in 2024. Her field of research studies centers on cellular and molecular biology. Her final paper examines the anticancer potential of jojoba seed oil, which aligns with her previous internship experience at Saraya Lab School of Pharmaceutical Sciences Osaka University in a research laboratory dedicated to studying the jojoba plant and oil. Vinka is currently preparing for future contributions to biotechnology and biomedical research.

# Anticancer Strategy Using Alcohol Metabolites via Therapeutic *In Vivo* Synthetic Chemistry

Koichi Ishida,[1] Yudai Ode,[1] Ambara R. Pradipta,[1] Tsung-che Chang,[2] Katsunori Tanaka[1,2]

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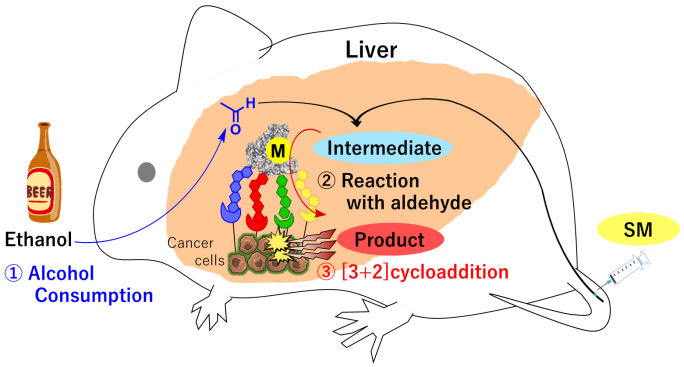
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

In cancer treatment, minimizing the impact on healthy tissues while administering anticancer drugs is crucial. Our laboratory conducts research to develop technology capable of generating drug molecules only at the cancer site. Through anchoring transition metal catalysts into the hydrophobic pocket of albumins to form artificial metalloenzymes (ArMs)[1], we successfully used the ArMs to synthesize various molecules in vivo. Moreover, we have demonstrated that glycoalbumins can have diverse organ- or cancer-targeting characteristics by modifying the glycan diversity of the albumin[2].

In this study, we developed a Lewis acid-based ArM. With a reported [3+2] cycloaddition, we successfully synthesized heterocyclic compounds from aldehydes and oximes in blood via the Lewis acid ArM. Acetaldehyde is a byproduct of alcohol consumption in vivo. With the metabolized acetaldehyde, we aim to synthesize anti-cancer compounds at cancer sites via the in vivo [3+2] cycloaddition. This approach is anticipated to be particularly effective in eradicating side effects, as the reaction is restricted to cancer cells exclusively.




*References*:
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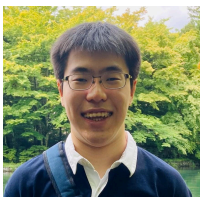
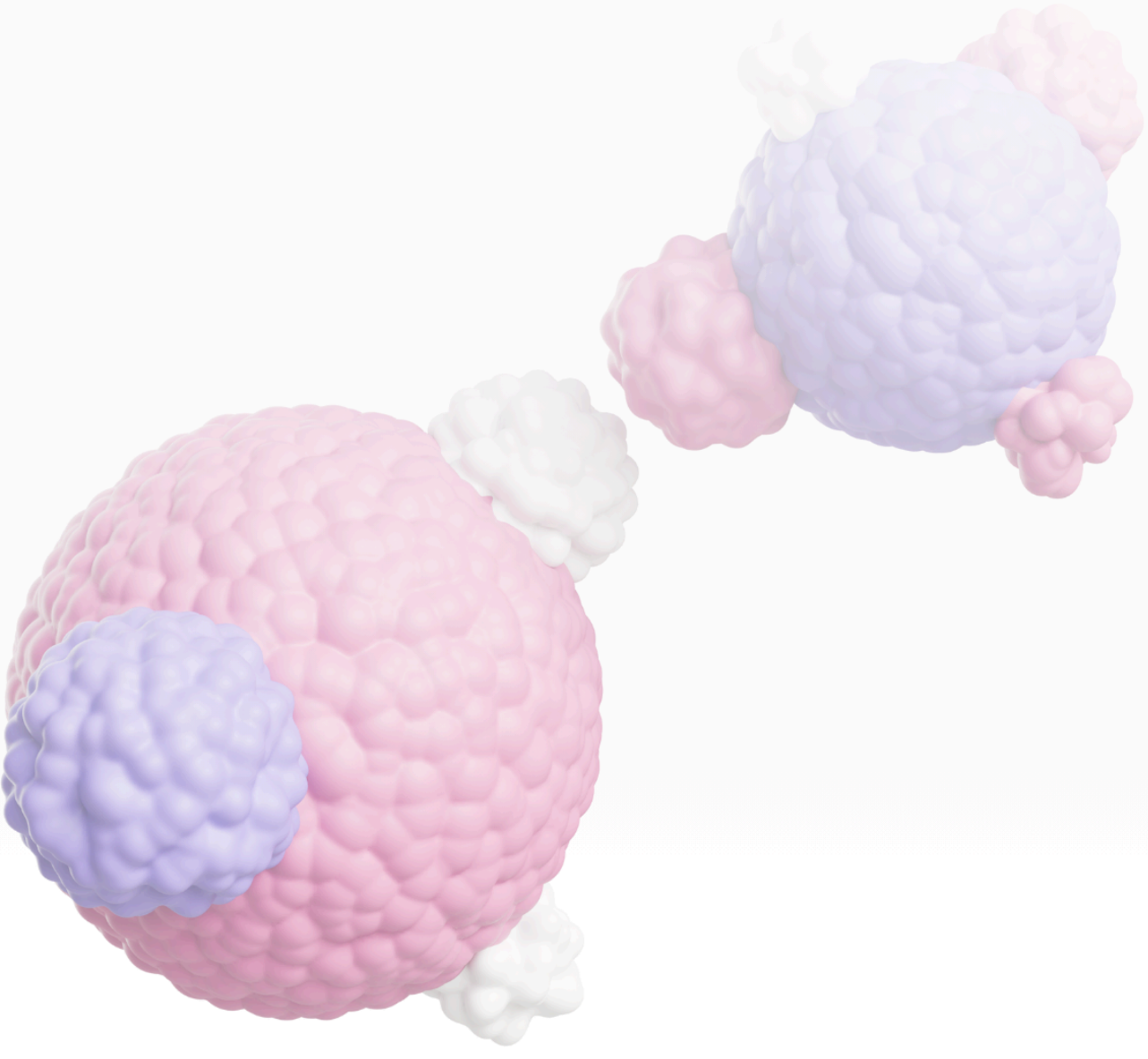


**Koichi Ishida**
*Master Student,*
*Tokyo Institute of Technology*

Koichi Ishida completed his undergraduate degree in the Department of Chemical Science and Engineering, Tokyo Institute of Technology, in 2023. He has been in a master's course since April 2023. His expertise lies in Organic Synthetic Chemistry, Artificial Metalloenzyme, and In Vivo Synthesis. His research focuses on *in vivo* synthesis of anticancer compounds via Lewis acid catalytic reaction using acetaldehyde metabolites from alcohol. In his free time, he enjoys musicals and reading.



# Isolation and Characterization of Circulating Tumor Cells Expressing Plastin-3 (PLS3) Using Density Gradient and Erythrolysis Methods.

Annisa R. Putri[1], Dimas R. Noor[3], Murdhani Abdullah[2,3], Fadhillah[1], Astari Dwiranti[1], Anom Bowolaksono[1]

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[3]Human Cancer Research Center, Indonesian Medical Education and Research Institute, Faculty of Medicine, Universitas Indonesia, Jakarta 10430, Indonesia

Circulating tumor cells (CTCs) present in the bloodstream of individuals with colorectal cancer can serve as an indication of their potential to develop metastases.[1] Immunomagnetic isolation, which depends on interactions between antibodies and epithelial-specific antigens, is widely used for detecting CTCs. However, this method may miss CTCs that have undergone epithelial-mesenchymal transition (EMT), as they lose epithelial properties and gain mesenchymal characteristics, making them less detectable by epithelial-specific markers.[2] Alternative methods with high capture sensitivity that rely on physical properties like density gradient and erythrolysis are developed.[3] Immunofluorescence staining characterizes CTCs based on molecular marker expression. Plastin-3 (PLS3) is a protein marker overexpressed in colorectal cancer CTCs undergoing EMT. [4] This study aims to isolate and characterize PLS3-expressing CTCs from colorectal cancer patients, comparing the erythrolysis and density gradient methods for isolation and characterization based on the number of isolated cells. Optimization and validation were performed with spike-in assays using HT-29 cells in healthy donor blood. Our study found that erythrolysis isolated more CTCs, with PLS3-expressing CTCs found in all subjects, both as single cells and clusters of varying shapes and sizes. We will present further insights and details of our findings in the upcoming symposium.

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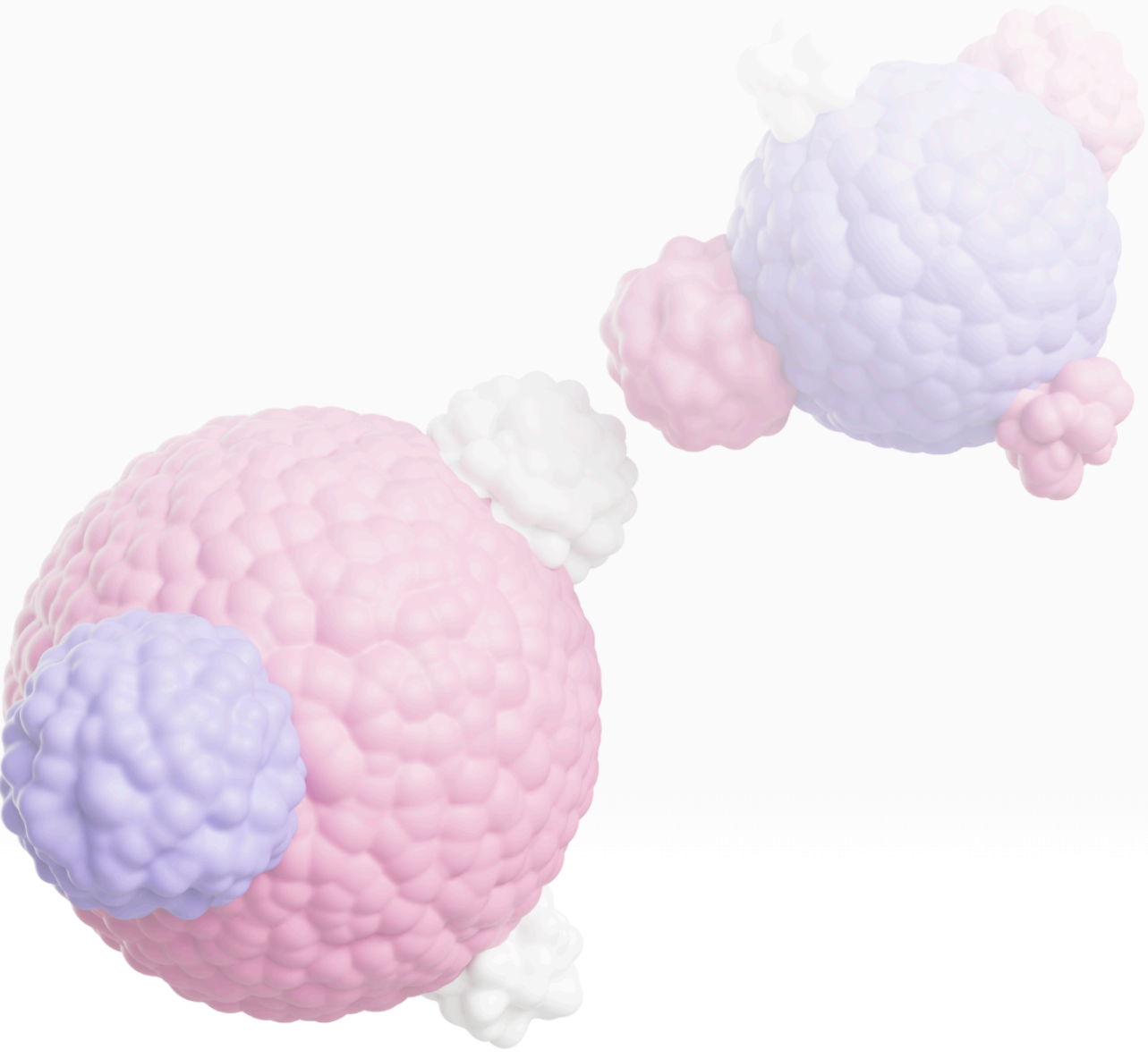
**Annisa Rahmani Putri**
*Student, Universitas Indonesia*

Annisa Rahmani Putri earned her Bachelor of Science in Biology from the Department of Biology, Universitas Indonesia. Her research studies is focused in the field of cellular and molecular biology, with her undergraduate thesis centered on methods for detecting circulating tumor cells in colorectal cancer. She has an interest in biomedical and biotechnology sciences. Currently, she is training as a research assistant, working on the formulation of tuberculosis vaccine agents research.



# Clinical Synthetic Chemistry: Rapid Intraoperative Diagnosis of Breast Cancer

Ambara R. Pradipta,[1] Motoko Fujii,[1] Katsunori Tanaka[1,2]

[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

Developing a highly accurate and rapid method for diagnosing breast cancer directly in the operating room is of utmost importance. The current histological analysis method employed for determining surgical margins is time-consuming, necessitating the need to develop a new intraoperative method. Acrolein, an unsaturated aldehyde, is a highly toxic environmental pollutant commonly found in tobacco smoke and exhaust gas. It is also ubiquitous in biosystems, where it is generated via the lipid peroxidation process and metabolism of polyamines. We recently found that [3+2] cycloaddition between aryl azide and acrolein that proceeds without a catalyst gives a diazo derivative even under physiological conditions. The method has been successfully utilized as a simple and robust method for detecting acrolein generated by live cells.[1]

This study utilized the azide-acrolein cycloaddition-based method to differentiate breast cancer lesions from normal breast gland tissue resected from breast cancer patients (Fig. 1). This is the first example of an organic synthetic chemistry-based approach that can be used to visualize cancer tissue and distinguish the morphology of the resected tissue within a few minutes.[2,3] This method has a potential clinical application for breast-conserving surgery. We will provide more information on these findings and their potential clinical applications in the symposium.

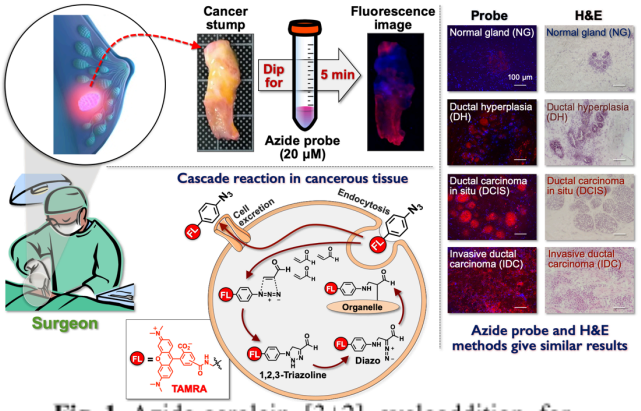



**Fig. 1** Azide-acrolein [3+2] cycloaddition for intraoperative diagnosis of breast cancer.

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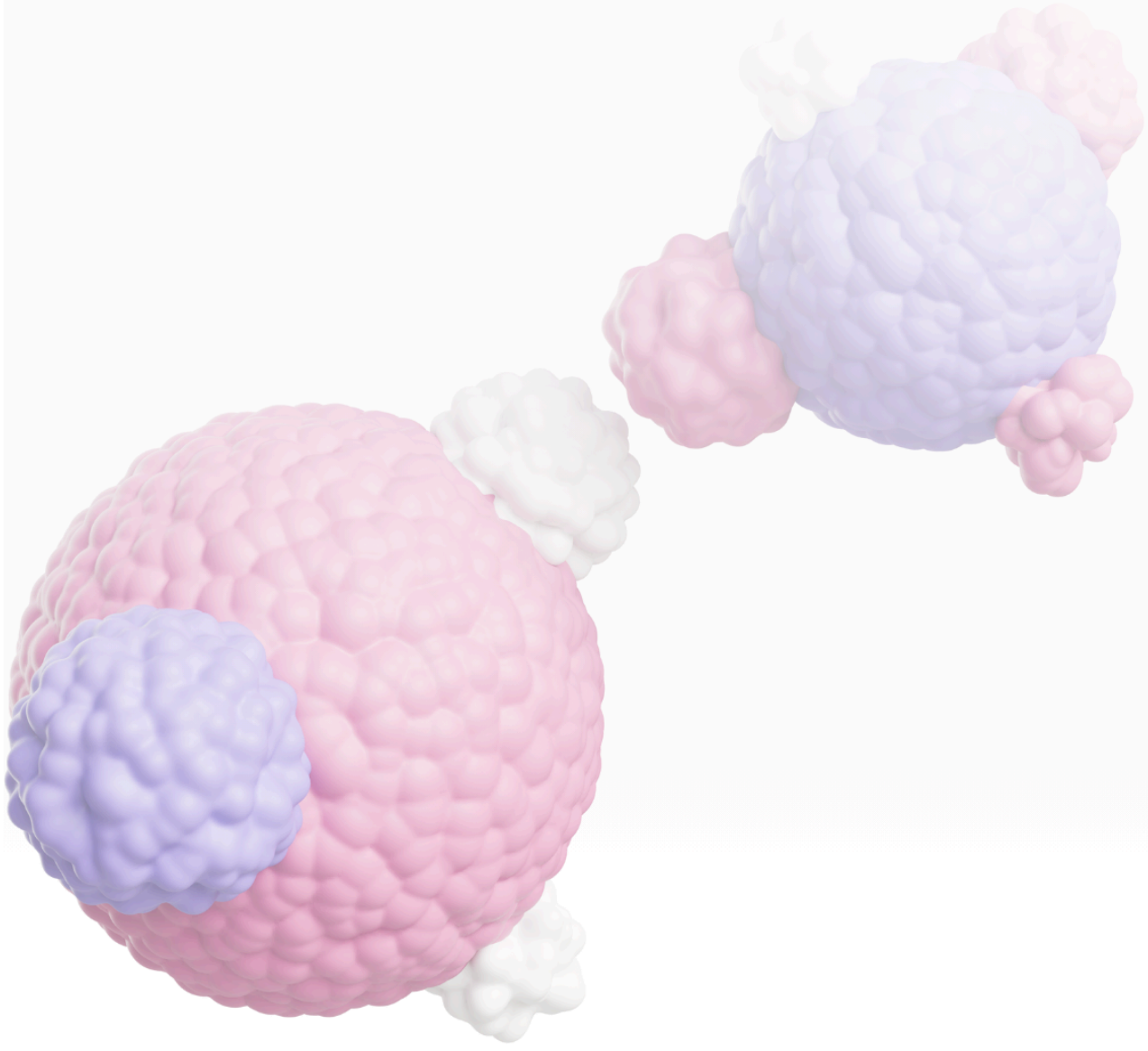
**Ambara R. Pradipta**
*Assistant Professor, Tokyo Institute of Technology*

Ambara R. Pradipta earned his Ph.D. in Chemistry from the Graduate School of Science at Osaka University in 2011. Following that, he worked as a postdoctoral researcher at Osaka University and as a special postdoctoral researcher at RIKEN. He has held his current position since April 2020. His expertise lies in bioorganic chemistry, organic synthesis chemistry, and natural product chemistry. His research is focused on developing advanced diagnostic and therapeutic methods by transforming metabolites from living organisms into diagnostic and therapeutic agents through organic synthesis chemistry. In his leisure time, he enjoys playing basketball and the acoustic guitar.



# Extrachromosomal DNA in Breast Cancer Cell Lines: Detection and Characterization

Shadira Anindieta Irdianto[1], Fadhilah[1], Retno Lestari[1], Fadilah[2], Anom Bowolaksono[1], Astari Dwiranti[1]

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[2]Department of Medical Chemistry, Faculty of Medicine, Universitas Indonesia, Central Jakarta 10430, Indonesia.

This study delves into the intriguing world of extrachromosomal DNA (ecDNA) in two distinct breast cancer cell lines: MDA-MB-231 (triple-negative) and MCF-7 (Luminal-A). Employing advanced imaging techniques, the research delineates notable differences in ecDNA quantity, distribution, and fluorescence intensity between these cell lines, suggesting a potential role of ecDNA in driving cancer aggressiveness.[1] The elevated levels of ecDNA observed in MDA-MB-231 cells may contribute to their enhanced metastatic potential.

Additionally, ultrastructural examination through scanning electron microscopy reveals that MDA-MB-231 cells have larger surface areas and greater fluorescence intensities of ecDNA compared to MCF-7 cells (Fig. 1). These findings indicate a potential association between ecDNA presence and genomic instability, as well as oncogene amplification in more aggressive cancer types.[2,3] These insights open new avenues for targeted cancer therapies, emphasizing the need to explore the mechanisms of ecDNA formation and its impact on cancer progression.

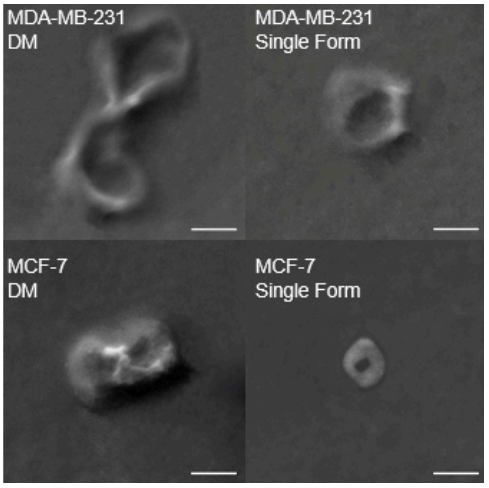


**Fig 1.** The ultrastructure of ecDNA

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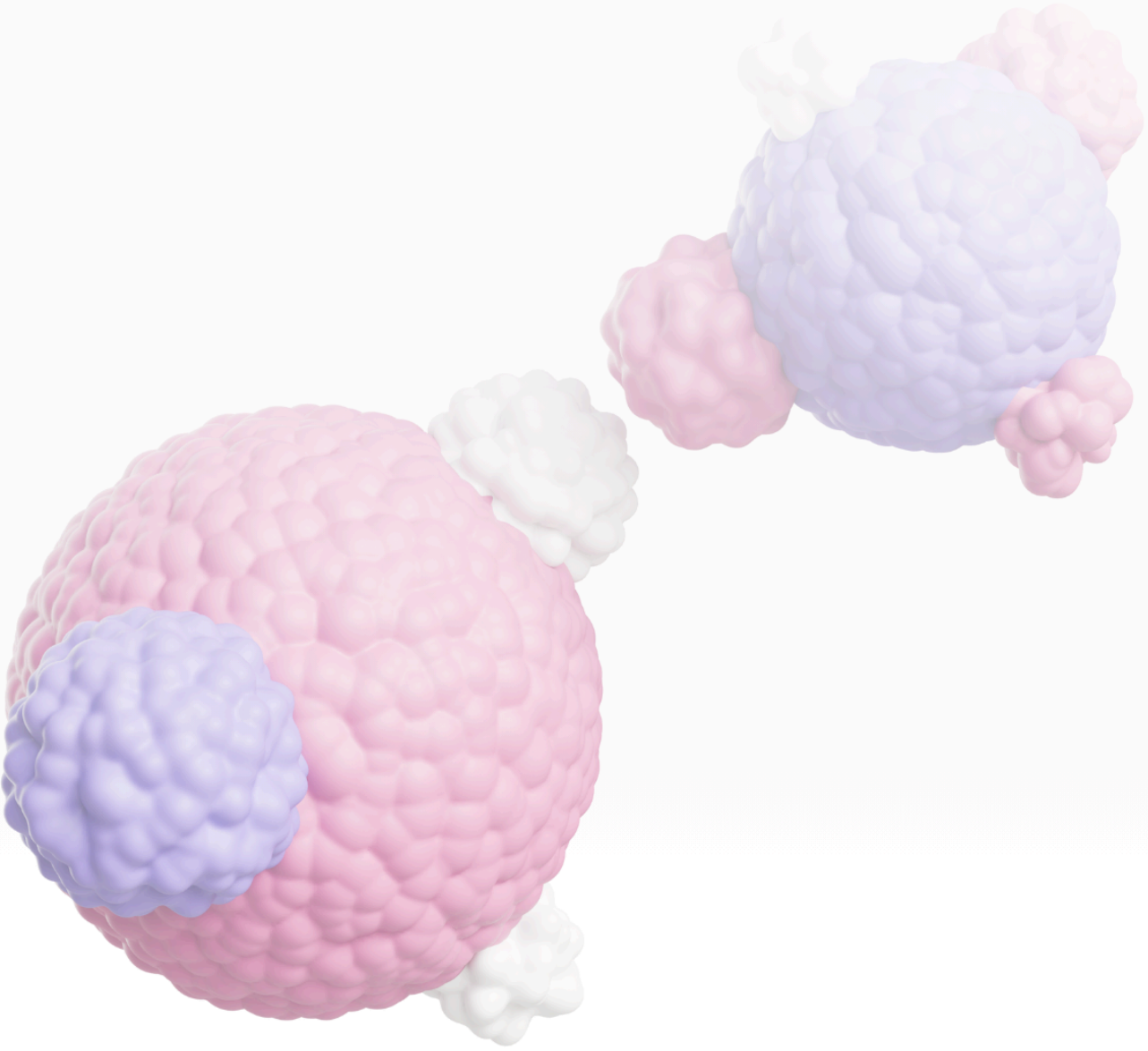
*Graduate Student,*
*Universitas Indonesia*

Shadira Anindieta Irdianto is a graduate student at the Department of Biology, Universitas Indonesia. She earned her bachelor's degree in 2023 with a focus on anticancer treatment using natural compounds, where she conducted significant research in this area. Currently, her academic and research interests have evolved towards studying extrachromosomal DNA (ecDNA), exploring its role in cancer biology and its potential as a target for therapeutic interventions. Through her work, she aims to contribute to a deeper understanding of cancer mechanisms and the development of innovative treatment strategies.



# Targeted Radioisotope Therapy via [3+2] Cycloaddition with Cancer Metabolites

Yudai Ode,[1] Akihiro Ishiwata,[2] Akiko Nakamura,[2] Yuriko Kusakari,[2]
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Targeted radioisotope therapy is a cancer treatment method in which radioactive isotopes (RIs) are attached to cancer-targeting molecules and used as therapeutic agents. For effective treatment, these agents must quickly reach the target cancer cells, be highly selective, and have a high retention rate. Our study introduces a new strategy for internal radiation therapy using organic reactions with endogenous acrolein produced in cancer cells and various RIs.

Our research has shown that acrolein, a highly reactive unsaturated aldehyde, is generated in high concentrations in various cancer cells irrespective of their subtypes. Our previous findings also demonstrate that fluorescence-labeled aryl azide molecules react with the endogenous acrolein within cancer cells through the [3+2] cycloaddition reaction, resulting in the effective retention of fluorescence within cancer cells. This phenomenon has been observed in tissue samples from cancer patients, and the method is currently used for cancer detection and differentiation in clinical samples.

Herein, we have designed aryl azide derivatives labeled with various metallic and non-metallic RIs that target the acrolein of cancer cells and have investigated their accumulation in cancer cells after the reaction with endogenous acrolein in vivo. Additionally, we have evaluated the therapeutic effects of this organic synthesis reaction-based method in the xenograft-mouse model.

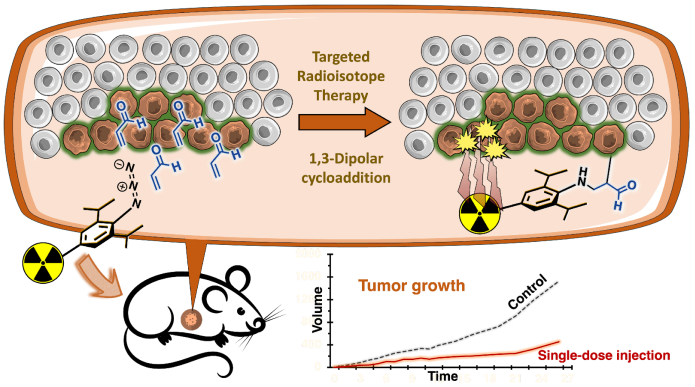


**Fig. 1** Targeted radioisotope therapy utilizing azide-acrolein reaction

*References*:
1. Y. Ode, A. R. Pradipta, P. Ahmadi, A. Ishiwata, A. Nakamura, Y. Egawa, Y. Kusakari, K. Muguruma, Y. Wang, X. Yin, N. Sato, H. Haba, K. Tanaka, *Chem. Sci.* **2023**, *14*, 8054.
2. Y. Ode, A. R. Pradipta, A. Ishiwata, A. Nambu, K. Ohnuki, H. Mizuma, H. Haba, K. Tanaka, *Chem. Commun*. **2024**, *60*, 3291.

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*Doctoral Student,*
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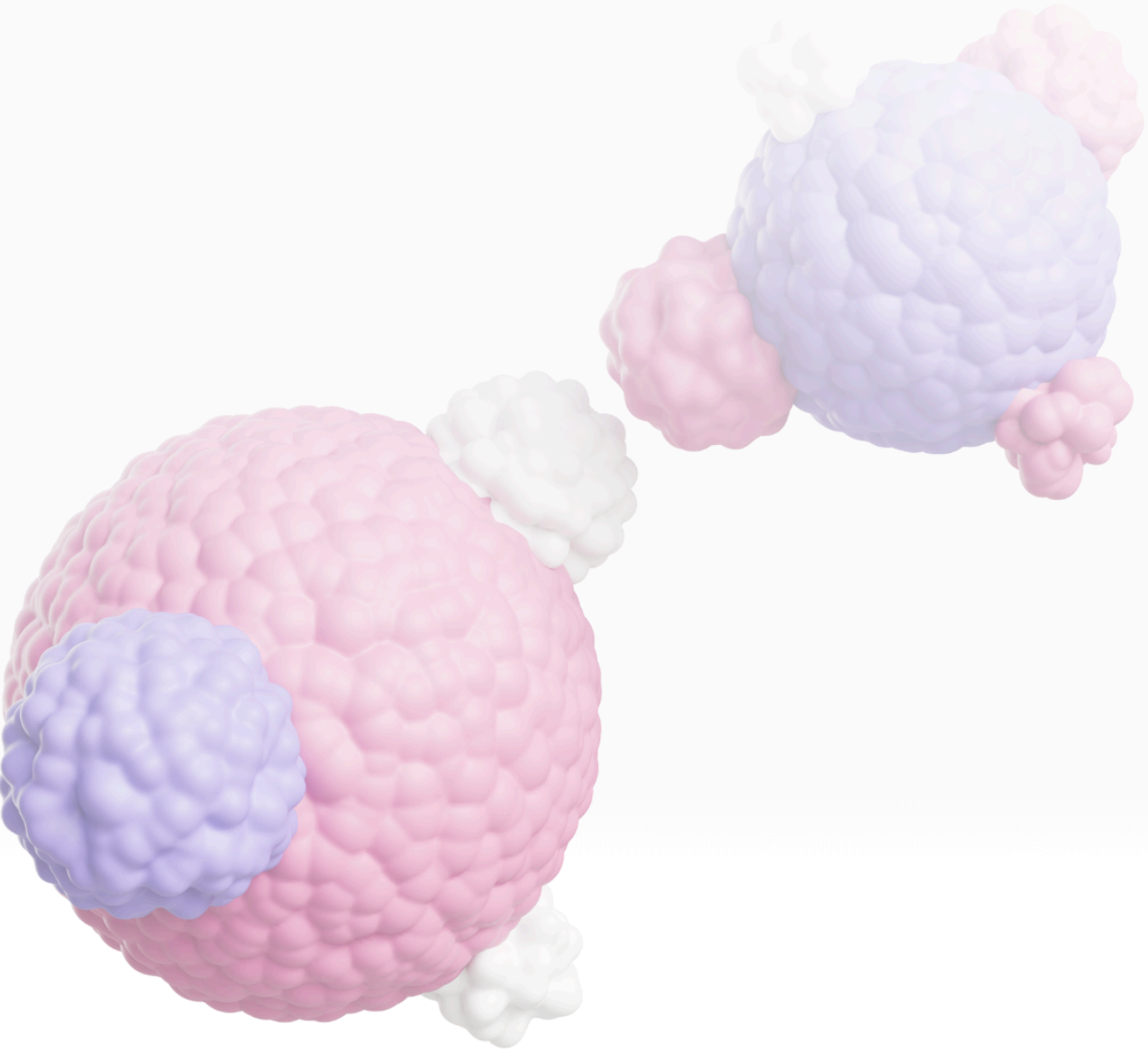
Yudai Ode is a third-year doctoral student in the Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology. His expertise lies in bioorganic chemistry, organic synthesis chemistry, and radiation chemistry. He specializes in bioorganic chemistry, synthetic organic chemistry, and radiation chemistry. His research interests include the use of radiation to achieve "Therapeutic In Vivo Synthetic Chemistry". In his free time, he enjoys playing music games (Dance Dance Revolution).



# In Vitro Screening of Several Indonesian Herb Extracts Against Dengue Virus Serotypes 2 and 4

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[2]Department of Biology, Faculty of Mathematics and Life Sciences, Depok, West Java, Indonesia

Recently, dengue infection has resulted in 88,593 cases and 621 fatalities in Indonesia, one of which was attributed to co-infection with DENV serotype 2 (DENV-2) and DENV serotype 4 (DENV-4). To date, vector control and restricted vaccination are the sole measures implemented to mitigate dengue cases. Antivirals may serve as an alternative; nevertheless, synthetic antivirals have proven ineffective. This study employs plant extracts that encompass bioactive components recognized as traditional remedies. The study seeks to ascertain the cytotoxicity value (CC50) and the potential antiviral efficacy against DENV-2 and DENV-4 of 10 extracts, comparing them with two extracts that have demonstrated efficacy as dengue antivirals. Twelve plant extracts were produced and evaluated using the MTT assay to determine cytotoxicity levels (CC50). The cytotoxicity values (CC50) revealed that eight extracts were non-toxic, at concentrations between 222.3 ppm and 5609.0 ppm, in comparison to positive controls of 151.7 ppm and 148.8 ppm. Three plant extracts showed efficacy as antivirals against both serotype viruses, whereas three extracts exhibited potential against one serotype virus, with inhibition activity from 50% to 100%. Nevertheless, four plant extracts exhibited no antiviral potential, as their inhibition percentages fell below 50%. *Sonchus arvensis*, *Kaempferia galanga*, *Curcuma aeruginosa*, *Syzygium polyanthum*, *Centella asiatica*, *Ardisia elliptica*, *Anredera cordifolia*, and *Sechium edule* were identified as non-toxic. *Syzygium polyanthum*, *Ardisia elliptica*, and *Anredera cordifolia* exhibit possible antiviral properties against DENV-2 and DENV-4.

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*Senior Researcher,*
Research Center for Vaccine and Drugs, BRIN

Sabar Pambudi completed his doctoral studies in Medical Science at Osaka University, Japan, and graduated in 2014. He is a senior researcher at the Research Center for Vaccine and Drug, BRIN, where his main research activities are the development of antigen and antibody monoclonals for infectious detection and screening Indonesian herb extracts for dengue antivirals.

# Synthesis of Functional Polymers in Cancer Cells via Uncatalyzed [4+4] Cycloaddition for Cancer-Selective Detection

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Compounds with eight-membered nitrogen-containing heterocycles are notable for their unique properties. However, their synthesis difficulties have limited further study despite their potential applications.

We previously discovered that when phenylglycinol reacts with acrolein, produced by cancer cells, it forms intermediate imines that undergo [4+4] cycloaddition to produce eight-membered ring compounds quantitatively (Fig. 1a).[1-3]

This research aims to synthesize an eight-membered nitrogen-containing heterocycles polymer through the reaction of phenylglycinol derivatives with acrolein (Fig. 1b). As acrolein is abundant in cancer cells, we propose the possibility of polymerization within this environment. Additionally, we have examined the potential of utilizing this reaction to create polymers suitable for cancer treatment and detection. Further details will be discussed at the symposium.

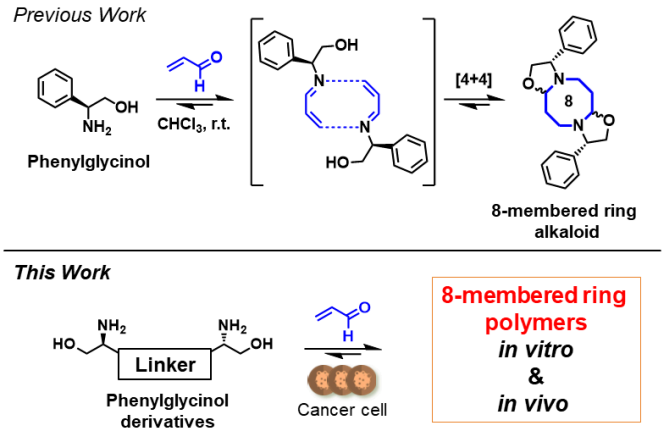


**Fig. 1** The [4+4] cycloaddition reaction.

*References*:
1. Tanei, T.; Tanaka, K. et al., *Adv. Sci.*, **2019**, *6*, 1801479.
2. Pradipta, A. R.; Tanaka, K. et al., *Synlett*, **2014**, *25*, 1026.
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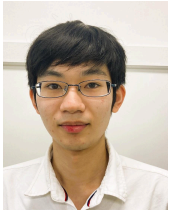

**Shinji Kawaguchi**
*Doctoral Student, Tokyo Institute of Technology*

Shinji Kawaguchi (川口 慎司). Tokyo Institute of Technology (M.Eng. (chemistry), Department of Chemical Science and Engineering, 2024). Current: 1st Year Student of Ph.D. Research field: Organic Synthetic Chemistry, *In vivo* Polymer Synthesis, Cancer Cell.
Hobbies and Interests: Mobile quiz game, Museum-hopping.

# Caffeine-induced Modulation of Cellular Death and Telomerase Activity in Breast Cancer Cells

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Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen (ER), progesterone (PR) receptors, and HER2 expression.[1] The MDA-MB-231 cells is commonly used as an in vitro model for identifying novel therapeutic agents for TNBC. Caffeine, a widely consumed stimulant, has shown promising anticancer effects, particularly in gastric cancer, where it promotes apoptosis and reduces telomerase activity.[2] However, studies on the effects of caffeine on MDA-MB-231 cells remain limited. This study aims to investigate the impact of caffeine concentrations (5, 10, 15, and 20 mM) on cell viability, apoptosis, and the expression of genes involved in apoptosis (*BAX, BCL2*, and *CASP8*) and telomerase activity (*hTERT*) in MDA-MB-231 cells. CCK-8 assay revealed a dose-dependent decrease in cell viability. Flow cytometry confirmed that caffeine induced apoptosis, particularly early-stage apoptosis. qPCR analysis showed a significant increase in the *BAX/BCL2* ratio at caffeine concentrations of 10 mM and above, indicating activation of the intrinsic apoptosis pathway. *CASP8* expression increased at 5 mM but decreased at higher concentrations (10–20 mM), suggesting a diminished role for the extrinsic apoptosis pathway. These findings indicate that caffeine potentially induces apoptosis without causing direct cell death, acting as a pro-apoptotic agent by modulating *BAX, BCL2*, and *CASP8* gene expression in MDA-MB-231 cells.

*References*: (1) Widiana, I. K., Irawan, H. Clinical and Subtypes of Breast Cancer in Indonesia. *Asian Pacific Journal of Cancer Care* **2020**, 5 (4). https://doi.org/10.31557/apjcc.2020.5.4.281-285. (2) Liu, H., Zhou, Y., Tang, L. Caffeine Induces Sustained Apoptosis of Human Gastric Cancer Cells by Activating the Caspase-9/Caspase-3 Signalling Pathway. *Mol Med Rep* **2017**, 16 (3). https://doi.org/10.3892/mmr.2017.6894.

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*Graduate Student,*
*Universitas Indonesia*

Qanita is currently pursuing a Master's degree in Biology at Universitas Indonesia. Her early research experience was shaped by her undergraduate thesis, which explored molecular markers in patient-derived breast cancer primary cultures. With expertise in cancer biology, molecular oncology, and cell biology, Qanita's current research centers on identifying novel therapeutic agents and unraveling their mechanisms of action in cancer treatment. Through her work, she aims to contribute to the development of innovative treatments that target the fundamental pathways driving cancer progression.

# Amidation with Polyamines generated in Cancer Cells for In Vivo Drug Synthesis

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Our laboratory is currently focusing on "Therapeutic In Vivo Synthetic Chemistry," which represents a departure from the traditional prodrug approach relying on deprotection for activation. In this innovative method, a drug precursor is introduced into a cell or body, and the drug's structure is directly synthesized at a specific site in vivo to diagnose and treat diseases.

It is well-documented that polyamines such as spermine and spermidine are produced at elevated levels in cancer cells.[1,2] Building upon our prior research, we have discovered that polyamines and molecules containing glycine propargylic ester can selectively react in water or organic solvents without necessitating coupling reagents or catalysts, efficiently forming amide bonds.[3,4]

Herein, our goal was to synthesize anti-cancer active molecules specifically within cancer cells through selective amidation reactions with polyamines, which are abundant in cancer cells, thus offering a potential cancer therapy approach with minimal side effects (Fig. 1). Essentially, we designed and synthesized various precursors based on the structures of natural toxic molecules and existing drug compounds. Upon administration of these precursors to cancer cells, we observed their conversion into anti-cancer active molecules within the cancer cells, exhibiting toxicity.

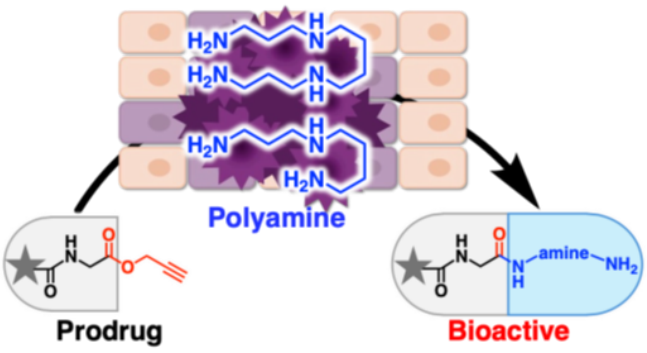


**Fig. SEQ Figure * ARABIC 1**
Research Scheme

*References*:
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2. K. Soda. *W'Waves* **2011**, *17*, 26.
3. K. K. H. Vong, S. Maeda, K. Tanaka. *Chem. Eur. J.* **2016**, *22*, 18865.
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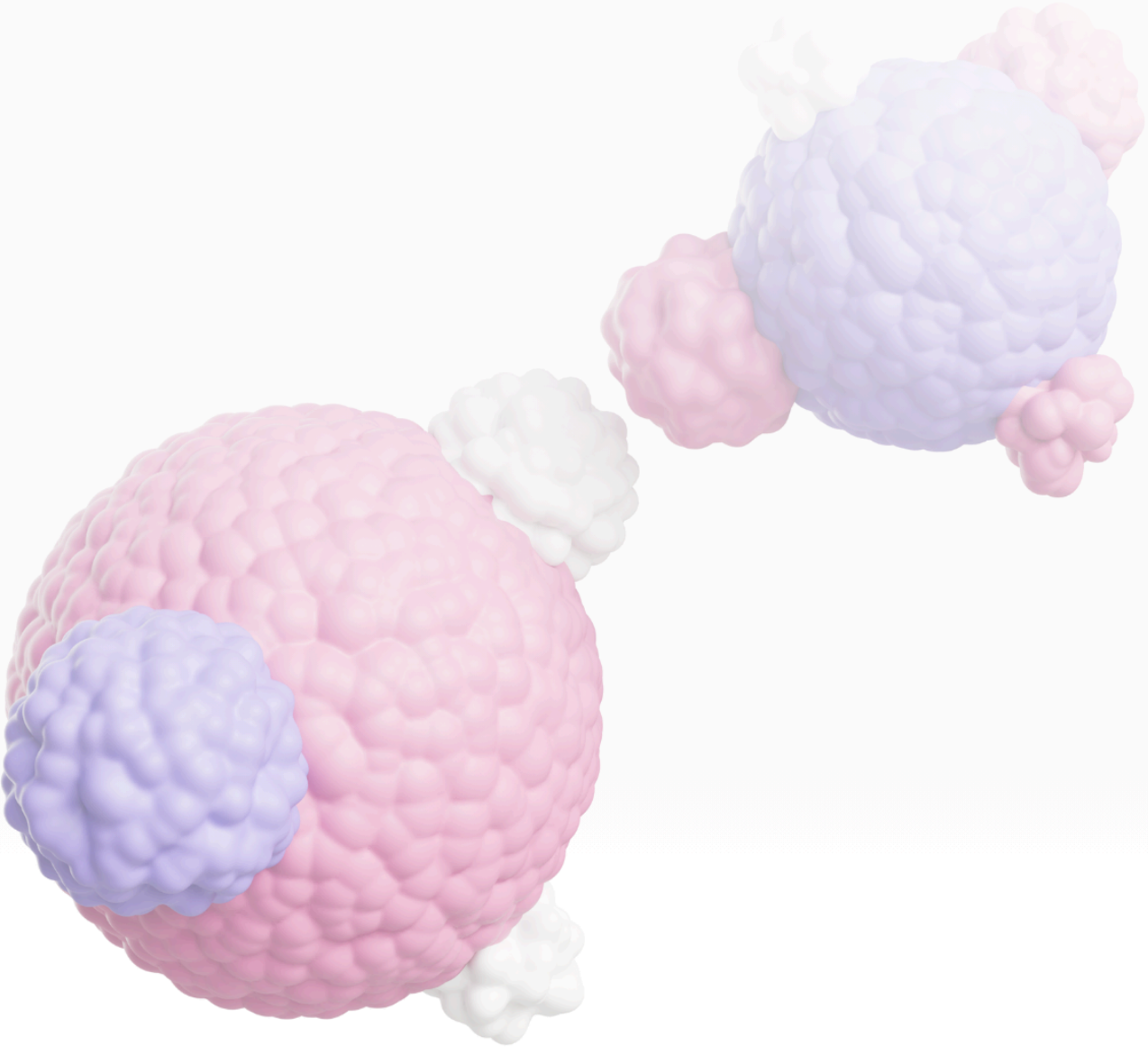
Atsuhiro Matsuura graduated from the Department of Materials Science and Engineering, Faculty of Engineering, Kyushu University in 2022.
At Kyushu University, he conducted research on “Diagnosis of Cancer using Human cell Orthogonal Enzymes”. Then, he moved to the Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, where he completed his master's degree in March 2024. He is currently enrolled in the doctoral program and is conducting research on cancer therapy by in vivo organic synthesis of anti-cancer drugs using polyamines. His hobbies are photography and cooking.



# Targeted Drug Synthesis in Cancer Cells via Palladium-catalyzed Reaction with Endogenous CO

Masayuki Kawai,[1] Tsung-Che Chang,[2] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

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Carbon monoxide (CO) is a commonly encountered toxic gas with unique properties. In organic chemistry, CO is a fundamental building block for producing carbonyl compounds. Interestingly, it occurs naturally in our bodies and plays essential roles in vasorelaxation and neurotransmission. Recent studies have identified an overexpression of CO in cancer cells.[1] Our study aimed to develop drug molecules within cancer cells using endogenous CO as a substrate, establishing a novel drug delivery system that does not rely on compound degradation or functional group deprotection reactions.

From the organic chemistry perspective, CO is not highly reactive towards organic compounds. This necessitates the use of transition metal catalysts such as palladium (Pd) in organic synthesis. However, catalyst poisons like glutathione make transition metal catalysts unsuitable for in vivo applications. To address this challenge, we designed an Albumin-Pd complex in which the metal catalyst is housed in a hydrophobic pocket of human serum albumin.[2] We successfully synthesized the Albumin-Pd complex and utilized it to convert endogenous CO generated by cancer cells into fluorescent molecules and drug molecules (Fig. 1). Further details will be presented at the symposium.

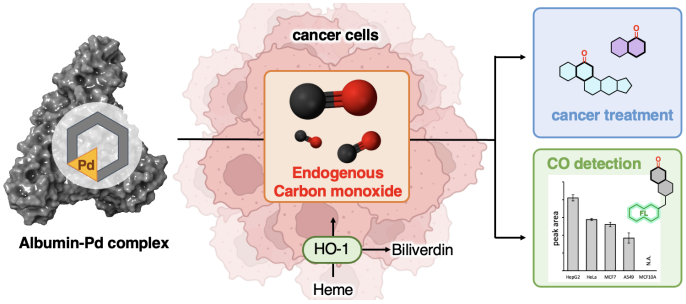


**Fig. 1** Conversion of endogenous CO into biofunctional molecules.

*References*:

1. S. Minegishi, A. Yumura, H. Miyoshi, S. Negi, S. Taketani, R. Motterlini, R. Foresti, K. Kano, H. Kitagishi, *J. Am. Chem. Soc.* **2017**, *139*, 5984.
2. I. Nasibullin, I. Smirnov, P. Ahmadi, K. Vong, A. Kurbangalieva, K. Tanaka, *Nature Commun.* **2022**, *13*, 39.

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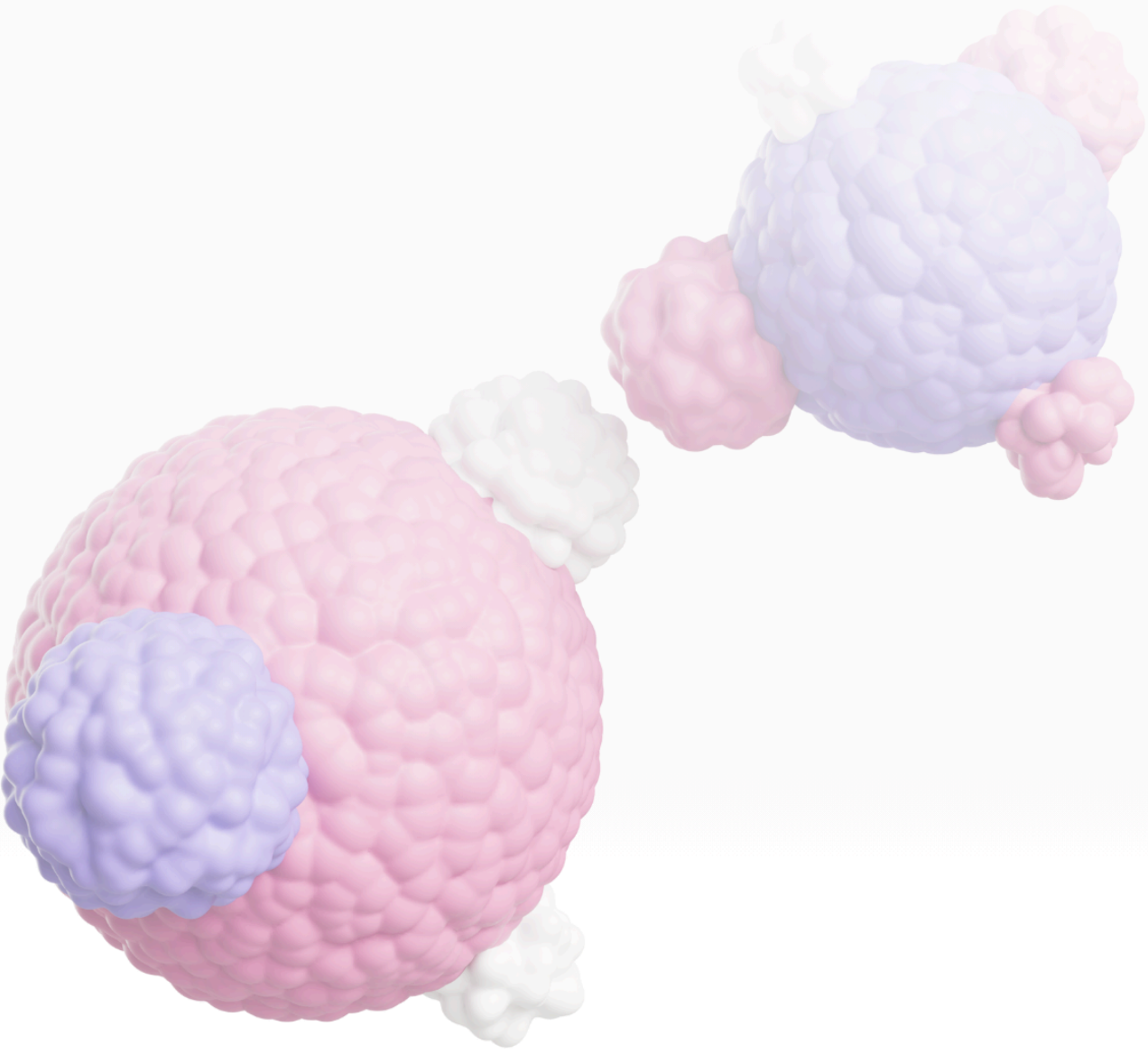
*Doctoral Student, Tokyo Institute of Technology*

Masayuki Kawai completed his master's course in the Department of Chemical Science and Engineering at the School of Materials and Chemical Technology, Tokyo Institute of Technology in 2024. His expertise lies in bioorganic chemistry, organic synthesis chemistry, and organometallic chemistry. His research focuses on cancer-targeted organic reaction through utilizing endogenous cancer metabolites by transition metal catalyst reaction. His hobby is marine sports and enjoys sailing and racing with friends.



# Hemin Enhances Aminolevulinic-Photodynamic Therapy (ALA-PDT) Effectiveness Through ABCG2 Downregulation

Rahma Wirdatul Umami[1], Anantya Pustimbara[2], Astari Dwiranti[1], Shun-Ichiro Ogura[2], Anom Bowolaksono[1]

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Aminolevulinic acid-mediated photodynamic therapy (ALA-PDT) is an effective cancer treatment with minimal side effects. This therapy utilizes ALA to induce selective accumulation of protoporphyrin IX, which is the key substance in the photodynamic reaction as it can trigger the formation of toxic reactive oxygen species within cancer cells [1]. However, ALA-PDT effectiveness can be reduced by ABCG2 and ABCB1 transporters hindering PpIX accumulation. Combining ALA with other substances can enhance PpIX accumulation [2]. Hemin is a potential substance due to its antitumor properties [3] and may affect ABCG2 and ABCB1 expression [4]. This study analyzed the effects of administering a combination of hemin and ALA after 48 hours on A549 lung cancer cells in vitro regarding cell viability, intracellular PpIX accumulation, *ABCG2, ABCB1* gene expression, as well as ABCG2 and ABCB1 protein expression. The results showed that the hemin combination could enhance the photodynamic therapy of ALA on A549 lung cancer cell line by affecting the cell viability, PpIX accumulation, gene expression, and protein expression. We will present further insights and details of our findings in the upcoming symposium.

References: (1) H. Mohammadpour & R. Fekrazad, R. *Photodiagnosis and photodynamic therapy.* **2016**, *14*, 200–203; (2) K. McNicholas, M. MacGregor & J. Gleadle. *British Journal of Cancer*, **2019**, *121*(8), 631–639; (3) Anselmino, N., Starbuck, M., Labanca, E., Cotignola, J., Navone, N., Gueron, G., Zenclussen, A. C., & Vazquez, E. *Antioxidants & redox signaling*. **2020**, *32*(17), 1243–1258 (4) Vesel, M., Rapp, J., Feller, D., Kiss, E., Jaromi, L., Meggyes, M., Miskei, G., Duga, B., Smuk, G., Laszlo, T., Karner, I., & Pongracz, J. E. *Respiratory research*. **2017** *18*(1), 52

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*Student, Universitas Indonesia*

Rahma Wirdatul Umami holds a Bachelor of Science in Biology from Universitas Indonesia, with research interests and experience in cellular and molecular biology, particularly in cancer research. She is passionate about advancing biomedical sciences, focusing on cellular mechanisms and innovations in cancer diagnosis and therapy

# Gold-Catalyzed Synthesis of Fluorescent Dyes Derived from Cancer Metabolites

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Fluorescent dyes, such as the aromatic heterocyclic compound Triazapentalene (TAP), are crucial in life sciences research. TAP, initially disclosed by Namba and co-workers in 2011, is known for its efficient synthesis and unique fluorescent properties.[1] Its small molecular size makes it particularly promising for applications in chemical biology. We have previously developed an efficient method to synthesize TAP through the gold-catalyzed reaction of triazoles obtained via the click reaction.

Our research aimed to synthesize the fluorescent dye TAP using endogenous acrolein directly in cancer cells. The synthesis utilizes an artificial metalloenzyme gold catalyst developed in our laboratory (Fig. 1).[2,3] The details will be discussed in the symposium.

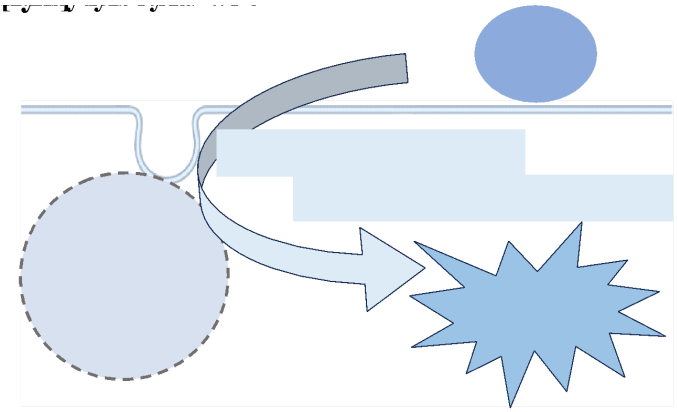

**Fig. 1** Synthesis the cancer cell-specific fluorescent dyes

*References*:
1. K. Namba, et al., *J. Am. Chem. Soc.* **2011**, *133*, 11466–11469.
2. K. Tanaka, et al., *Chem. Sci.*, **2021**, *12*, 5438.
3. K. Tanaka, et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12446–12454.

**Shunya Ohara**

*Doctoral Student, Tokyo Institute of Technology*

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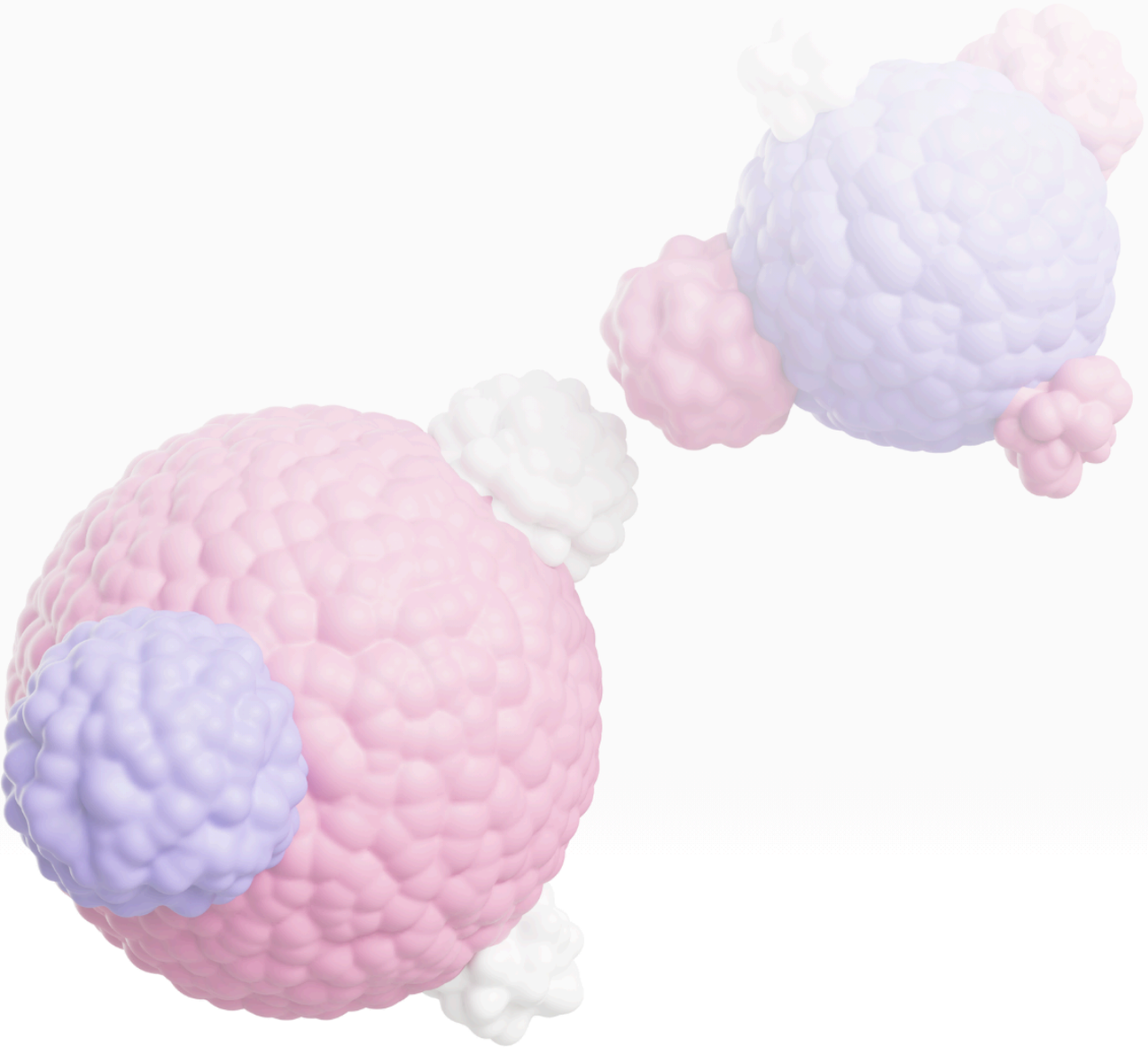
Tokyo University of Agriculture (B.Eng. Department of Life Sciences, 2024). Current: 1st Year Student of Doctoral Course.
Research field: Organic Synthetic Chemistry, Artificial Metalloenzyme, In vivo Synthesis.
Hobbies and Interests: Soccer, Golf



# Cloning and Expression of SCAMP3 in *Escherichia coli* BL21(DE3) as an Inducer of anti-SCAMP3 Monoclonal Antibody Production for Cancer Detection

Selly S. Rajagukguk[1], Sabar Pambudi[2], Astari Dwiranti[1], Anom Bowolaksono[1]

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Secretory Carrier Membrane Protein 3 (SCAMP3) is a crucial membrane protein involved in intracellular vesicle trafficking and exocytosis. SCAMP3 expression has been observed in various cancer types, such as melanoma, glioma, hepatocellular carcinoma and breast cancer. Studies have reported increased SCAMP3 expression in certain cancer cells compared to normal cells, suggesting a potential role for SCAMP3 in cancer development and progression. The study aims to further explore SCAMP3's function by cloning and expressing it in the bacterium *Escherichia coli* strain BL21(DE3). To achieve this, we amplified the *SCAMP3* gene and inserted it into a prokaryotic expression vector called pET21d(+). The recombinant plasmid was then introduced into *E. coli* cells for protein expression. SDS-PAGE and Western blotting was carried out to detect the expression product which was induced by IPTG and confirmed the present of a recombinant pET21d(+)-SCAMP3 at 38 kDA protein weight (Fig 1).

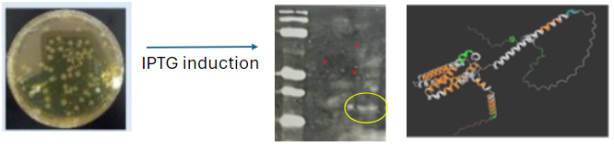


Fig 1. Expression of SCAMP3 in BL21(DE3) inducted by IPTG and the predicted of 3D protein conformation of SCAMP3

*References*: (1) James, S & Jain, V. 2022. Frontiers in bioengineering and biotechnology. 9(776828): 1 – 9. (2) Mishra, S. & Gomase, V.S. 2015. *Int.Journ.Adv Tech Eng Sci.* **3**(1): 28 – 36. (3) Thomas, P., Wohlford D., Aoh, Q.L. 2006. Bi*ochem.Biophys.Res.Comm.* **478**(3): 1028 – 1034.

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Selly S. Rajagukguk is a PhD candidate in the Department of Biology, University of Indonesia. Her current research focuses on biomedical sciences, with particular interests in molecular genetics, oncology, and immunology.

# Therapeutic In Vivo Synthetic Chemistry Using a Novel Anticancer Compound Derived from Bracken Poison

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Ptaquiloside is a norsesquiterpene glucoside found in bracken which shows carcinogenicity.[1] Its carcinogenic mechanism reveals that the intermediate **1**, generated through the hydrolysis and dehydration of Ptaquiloside, is a strong electrophile that reacts directly with biological nucleophiles, including amino acids and nucleotides, leading to damaged cells (Figure 1). Based on this fact, we consider that selective generation of **1** in cancer sites may be used for an anticancer approach. To achieve this purpose, a reliable method to synthesize the highly reactive **1** in biological systems is necessary.

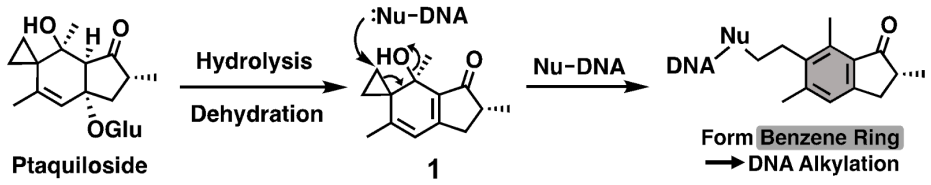



**Fig. 1** The carcinogenic mechanism of Ptaquiloside

Previously, we have found that metal catalysts can be used even in the *in vivo* by coordinating metal catalysts in the hydrophobic pocket of albumin. This protein-metal complex is called Artificial Metalloenzyme (ArM). Moreover, by modifying the surface of ArM with glycans, we succeeded in selectively accumulating ArM in cancer and conducting metal catalyzed reaction at cancer.[2]

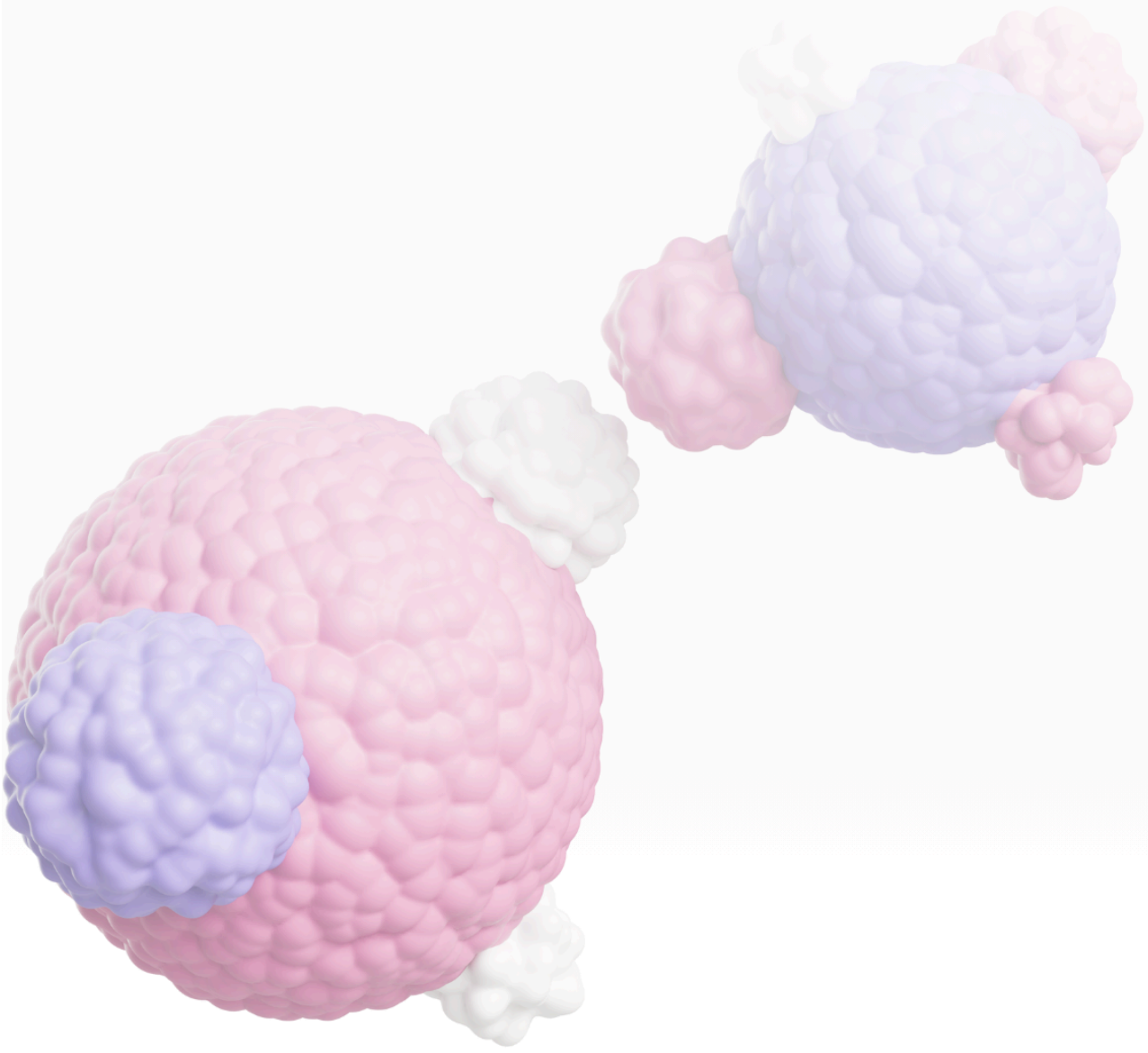
In this study, we have developed a method to synthesize **1** from its analog using a Ru catalyst-based ArM. Together with cancer-targeting glycans, we anticipate utilizing this approach for cancer treatment without inducing unwanted side effects. We will report the synthesis of the analog of **1** and its activity evaluation.

*References*:

1. K. Yamada, M. Ojika, H. Kigoshi, *Natural Product Reports*, **2007**, *24*, 798.
2. I. Nasibullin, I. Smirnov, P. Ahmadi, K. Vong, A. Kurbangalieva, K. Tanaka, *Nature Commun.*, **2022**, *13*, 39.

**Tatsuya Kobayashi**
*Master Student,*
*Tokyo Institute of Technology*

Tatsuya Kobayashi is second year of graduate student in the Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology. He completed his bachelor studies in the same institution in 2023. He will go to doctor course in the next year. His expertise lies in organic synthesis chemistry, and chemical biology. His research focuses on "organic synthesis chemistry *in vivo*". In his free time, he enjoys reading Japanese Manga and studying about poison.

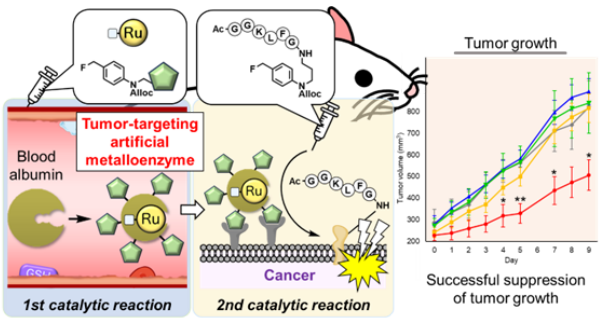


# Resourcing Mouse Blood Albumin as a Biocompatible Artificial Metalloenzyme for Colorectal Cancer Therapy

Kyosuke Imai,[1] Kyohei Muguruma,[2] Akiko Nakamura,[2] Yuriko Kusakari,[2] Tsung-Che Chang,[2] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

Many currently used anticancer drugs pose a risk of side effects as they not only harm cancer cells but also normal cells. To address this issue, targeted therapy using prodrugs is being explored as a potential method. Our recent report highlighted two key findings: (1) a transition metal catalyst with the albumin-binding ligand 7-diethylaminocoumarin can be integrated into albumin's hydrophobic pocket to create an Artificial Metalloenzyme (ArM), and (2) by further modifying the ArM with tumor-targeting molecules such as peptides or glycans, the ArM can be transformed into tumor-targeting ArMs that specifically target tumors and shield the catalyst. Subsequently, we conducted a metal-catalyzed reaction in mice using the tumor-targeting ArM to treat cancers.[1,2]




Here, we attempted to synthesize the tumor-targeting ArM directly in a live mouse using circulating albumin, which is abundant in the bloodstream (Fig. 1).[3] The details of the research will be discussed in the symposium.

**Fig.1** *In vivo* synthesis of tumor-targeting ArM from blood albumin

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1. P. Ahmadi, K. Muguruma, T.-C. Chang, S. Tamura, K. Tsubokura, Y. Egawa, T. Suzuki, N. Dohmae, Y. Nakao, K. Tanaka, *Chem. Sci.*, **2021**, 12, 12266.
2. I. Nasibullin, I. Smirnov, P. Ahmadi, K. Vong, A. Kurbangalieva, K. Tanaka, *Nature Commun.*, **2022**, 13, 39.
3. K. Imai, K. Muguruma, A. Nakamura, Y. Kusakari, T.-C. Chang, A. R. Pradipta, K. Tanaka, *Angew. Chem. Int. Ed.*, **2024** e202411225.

**Kyosuke Imai**
*Doctoral Student, Tokyo Institute of Technology*

Kyosuke Imai got a master's degree in the Department of Chemical Science and Engineering, Tokyo Institute of Technology in 2024. Afterward, he is studying about organic synthetic chemistry, artificial metalloenzyme and *in vivo* synthesis as a doctoral student in the same university. His research focuses on developing therapeutic methods by converting endogenous proteins into biocompatible artificial metalloenzyme and paving the way for the development of "therapeutic *in vivo* synthetic chemistry" strategies by replacing the administration of biologically derived proteins with small- to mid-sized molecules. In his free time, he enjoys jogging.

# Natural Solutions to Alleviate Signs of Dermal Ageing

Anom Bowolaksono[1]

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Signs of dermal ageing are the manifestation of accumulated changes on the structure, physiology, and cellular metabolism of dermal layer in human skin. These changes have been reported as the result of variation in genetic composition and the constant exposure of environmental stressors, such as air pollutant, sun rays, and unhealthy dietary intake which may lead to the uncontrolled deposition of advanced glycation end-products (AGE). The accumulation of AGE in human skin has serious implication in the emergence of early skin ageing signs by disrupting dermal fibroblast proliferation and increased the glycation of extracellular matrix (ECM). In the early part of the project, we are interested to discover the potential biomarkers to minimize the risk of early skin aging by understanding the pathophysiology of dermal ageing due to the accumulation of AGE by observing changes in cell viability, ROS production, DNA damage events, and the cell's mechanism to incorporate AGE molecules internally. The long-term objective of this project is to discover small molecule compounds which can target these biomarkers. This project is our effort to harness the full potential of rich selection of natural resources native from Indonesia as agents to regulate the expression of specific genes, thereby offering a sustainable approach to minimize the early signs of ageing in the dermal layer of human skin.

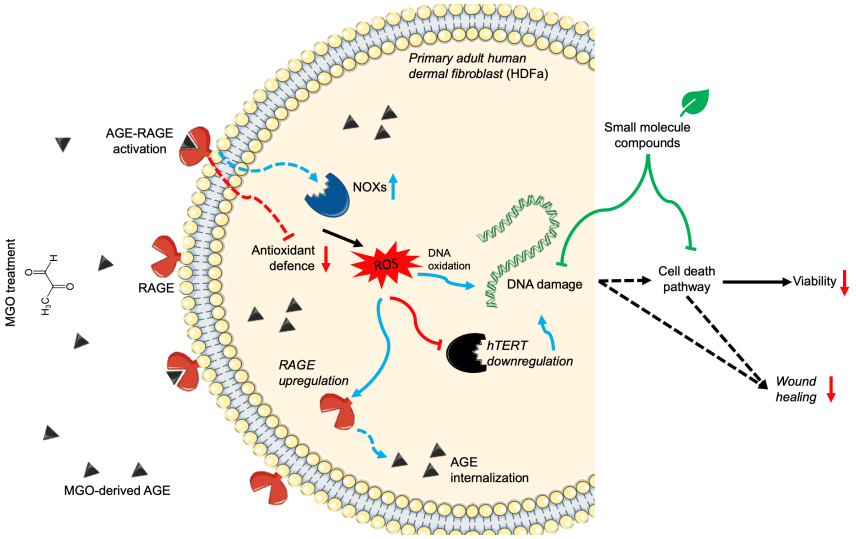


**Figure 1.** Illustration of a possible mechanism of cellular ageing due to AGE in human dermal fibroblast

**Prof. Anom Bowolaksono, Ph.D.**
*Professor*
*Universitas Indonesia*

Anom Bowolaksono, Ph.D. is a Professor at the Department of Biology, Universitas Indonesia. With a Ph.D. in Reproductive Biology from Okayama University, his research focus is on reproductive biology, aging, and apoptosis research. He earned his professor title in 2023.

# Effect of Caffeine on Cell Viability and *hTERT* Gene Expression in A549 Lung Cancer Cells

Yasmin Verena Jerissia Murtagh,[1] Astari Dwiranti,[1] Anom Bowolaksono[1]

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Lung cancer causes about 20% of all cancer-related deaths. Caffeine, a psychoactive substance widely consumed, has been found to affect areas other than the brain, including potential medical applications. Research shows caffeine can increase *hTERT* gene expression in MCF-7 and Hep-G2 cells (1). The *hTERT* gene regulates the *hTERT* protein, which elongates telomeres via telomerase, an enzyme abundant in cancer tumors. Telomere length is significant in cancer and anti-aging. There are several diseases related to telomere length, particularly degenerative diseases, such as Idiopathic Pulmonary Fibrosis (IPF), where patients exhibit shortened telomeres in alveolar epithelial cells in the lungs (2). qRT-PCR was used to detect *hTERT* gene expression, and the Trypan Blue Assay to detect cell viability. A549 cells were treated with caffeine powder diluted in Phosphate Buffered Saline (PBS) for 24 hours at concentrations of 0.5, 1, 2, 3, and 5 mM. qRT-PCR results showed increased *hTERT* expression after treatment with 0.5, 2, and 3 mM of caffeine but decreased expression after treatment with 1 and 5 mM caffeine. This is likely explained by cytotoxicity and TAK1 pathway activation (3). The Trypan Blue Assay showed a steady increase in A549 cell death with higher caffeine dosages. The decrease in gene expression and cell viability may be connected due to lower gene expression in less viable cells. Caffeine is an inducer of apoptosis by limiting BCL2 function, which likely explains this (4).

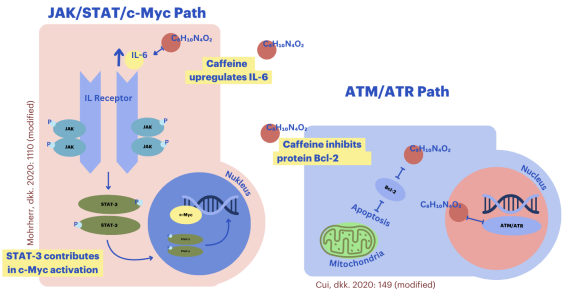
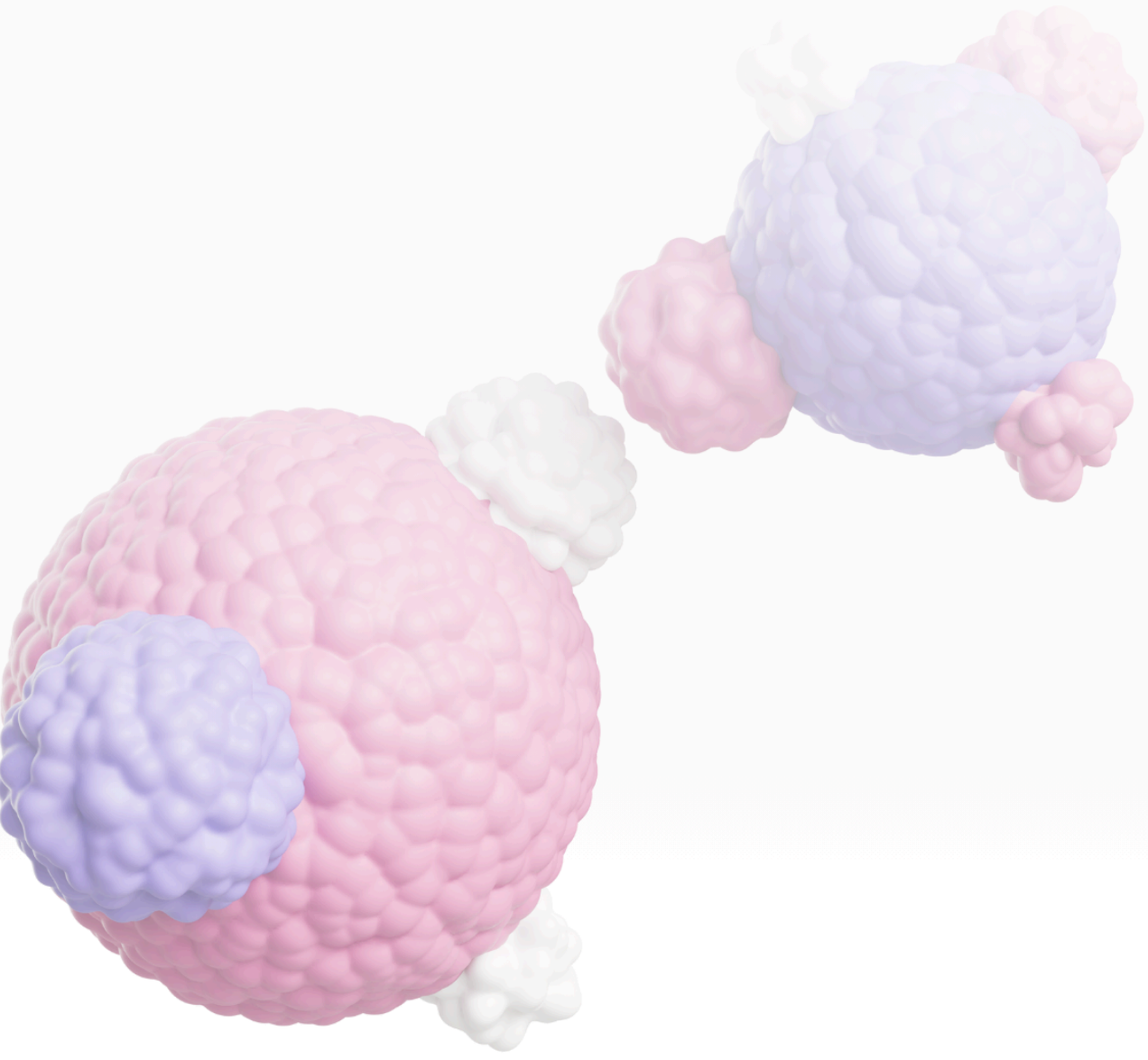



**Fig. 1** The role of caffeine in JAK/STAT/c-Myc and ATM/ATR pathways

Diao. 2021. Caffeine promotes the expression of telomerase reverse transcriptase to regulate cellular senescence and aging. *Food & Function* **12**(7): 2914–2924; (2) Barratt, S., A. Creamer, C. Hayton, & N. Chaudhuri. 2018. Idiopathic Pulmonary Fibrosis (IPF): An Overview. *Journal of Clinical Medicine* **7**(8): 201; (3) Fujiki, T., T. Miura, M. Maura, H. Shiraishi, S. Nishimura, Y. Imada, N. Uehara, K. Tashiro, S. Shirahata, & Y. Katakura. 2007. TAK1 represses transcription of the human telomerase reverse transcriptase gene. *Oncogene* **26**(36): 5258– 5266.; (4) Cui, W. -Q., S. -T. Wang, D. Pan, B. Chang, & L. -X. Sang. 2020. Caffeine and its main targets of colorectal cancer. *World Journal of Gastrointestinal Oncology* **12**(2): 149–172.

**Yasmin V. J. Murtagh**
*Student Researcher,*
*Universitas Indonesia*

Yasmin V. J. Murtagh is a recent undergraduate at Universitas Indonesia, majoring in Biology at the faculty of Mathematics and Natural Sciences. During her time there, she completed a research internship at the Graduate School of Biosciences, Kyoto university, shadowing Professor Kazuhiro Sakamaki at his laboratory, focusing on apoptosis. Following this, she completed another research internship at the Indonesia Medical Education and Research Institute, faculty of Medicine, Universitas Indonesia, before beginning her graduating research project, about the effects of caffeine on A549 lung cancer cells.



# The Roles of Butyrate in Inflammatory Orbital Fibroblast from Graves' Ophthalmopathy

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[1]Department of Biology, Faculty of Mathematics and Natural Science, Universitas Indonesia, Beji, Depok, Jawa Barat 16424, Indonesia
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Graves' Ophthalmopathy (GO) is an autoimmune disorder affecting orbital tissues, often inadequately managed by current treatments. This study explores the potential of butyrate, a gut microbiota metabolite, to modulate inflammation in orbital fibroblasts from GO patients[1]. Known for its histone deacetylase inhibition, butyrate may reduce inflammation by impacting IL-6 cytokine levels, a key inflammatory marker in GO[2]. In a 3D cell culture model, GO orbital fibroblasts were treated under four conditions: Control, PDGF-BB (to induce inflammation), Butyrate alone, and PDGF-BB + Butyrate. IL-6 levels were measured via ELISA across different time points. Results showed that PDGF-BB significantly elevated IL-6, with peak expression at 48 hours. Butyrate alone reduced IL-6 compared to control, and its addition to PDGF-BB lowered IL-6 levels significantly relative to PDGF-BB-only treatments, with the greatest effect at 72 hours. These findings suggest that butyrate could mitigate inflammation in GO, highlighting its potential as an adjunct therapy. Further in vivo studies are warranted to confirm its clinical relevance.

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*Undergraduate Student*
*Universitas Indonesia*

Rafi is a final-year student from the Department of Biology, Faculty of Mathematics and Natural Science, Universitas Indonesia, with a focus on cellular and molecular biology. The following research was conducted during his internship at Chulalongkorn University, Thailand, where he studied the roles of butyrate in inflammatory conditions. Currently, Rafi is working on his thesis, investigating the effects of Platelet-rich Plasma (PRP) on diabetic wound healing, focusing on inflammation mechanisms and gene expression in fibroblast cells. He has a strong interest in bioinformatics and synthetic biology, using data-driven approaches to address biological problems and exploring innovative solutions as reflected in his involvement in multiple synthetic biology initiatives.

# Effect of Inhibitor BIX01294 in Inhibiting EHMT1 and EHMT2 Gene Expression in A549 Lung Cancer Cells

Azka Alfathi Madani[1], D.S. Ramadhan[1], A.F. Hannaum[1], A. Bowolaksono[1]*, A. Dwiranti[1]

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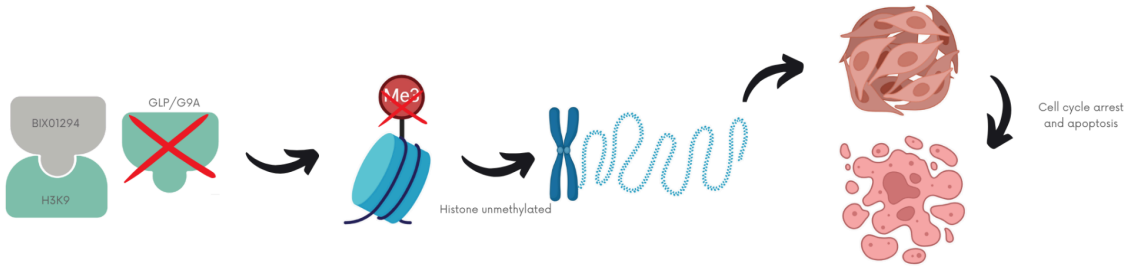
Epigenetic changes contribute to cancer malignancies by distrupting gene expression. Methylation is one of epigenetic changes that modifying histone that made expression become silenced. EHMT is associated to methylation on histone thus make chromatin become compact and inaccessible for gene expression. BIX01294 is an inhibitor of EHMT by competing the actual substrate, namely H3K9. BIX01294 is proven attenuates cancer cell proliferation on breast cancer, colorectal cancer, and prostate cancer by inhibiting EHMT1 activity. In this further study, BIX01294 is effective to inhibit EHMT1 and EHMT2 activity on A549 lung cancer cells by dose dependent manner.

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**Azka Alfathi Madani**
*Undergraduate Student*
*Universitas Indonesia*

Azka Alfathi Madani is an undergraduate student from Biology major in Universitas Indonesia. He was a trainee during research internship in Integrative Bioanalytics Laboratory at Tohoku University. His laboratory work is inspired and honed by his supervisor and mentors, Kawaoka Shinpei, Mayuko Yoda, and Don Saldajeno. Now, he tries to accomplish his degree and prepares to continue his study in Japan.

# Effect of Jojoba (*Simmondsia chinensis* (Link) Schneider) Seed Oil Towards the Viability, Apoptosis, and Ultrastructure of Breast Cancer MDA-MB-231

Frieska Amelia Widya Ananda,[1] Anom Bowolaksono,[1] Astari Dwiranti[1]

[1]Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, 16424, Indonesia

Breast cancer is one of the most impactful types of cancer globally.[1] Currently, breast cancer treatments are primarily limited to chemotherapy, which poses severe side effects to the body.[2] Jojoba (*Simmondsia chinensis* (Link) Schneider) seed oil is known to contain bioactive compounds, such as simmondsin, quinones, and phenolics, with potential anticancer properties, making it a promising candidate for natural treatment.[3] However, no research has yet explored the cytotoxic effects of jojoba seed oil on MDA-MB-231 breast cancer cells, which are known for their aggressiveness. This study aims to evaluate the cytotoxic effects of jojoba seed oil on the viability, apoptosis, and ultrastructure of MDA-MB-231 cells. Cell viability was assessed using the trypan blue assay, apoptosis was measured through flow cytometry, and ultrastructural changes were observed with Scanning Electron Microscopy (SEM). The analysis indicated the lowest viability at a concentration of 200 µg/mL. Apoptosis results showed the highest total apoptosis at a concentration of 400 µg/mL, demonstrating a dose-dependent cytotoxic effect. Additionally, SEM analysis revealed ultrastructural changes, including cell shrinkage and blebbing, which are characteristic features of apoptosis. Overall, the tests indicated decreased viability, increased apoptosis, and ultrastructural alterations in MDA-MB-231 cells.

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**Frieska Amelia W.A.**
*Student Researcher,*
*Universitas Indonesia*

Frieska Amelia W. A. recently completed her undergraduate degree in Biology at Universitas Indonesia, specializing in molecular biology with a focus on cell culture viability, toxicity testing, and gene and protein expression analysis. Her thesis explored the potential of jojoba seed oil as an anticancer agent for breast cancer. Known for her attention to detail, analytical skills, and proactive approach, Frieska is also actively involved in social and organizational activities, demonstrating her commitment to growth in both her professional and personal life.

# Jojoba (*Simmondsia chinensis* (Link) Schneider) Seed Oil Effect on the Viability and Ultrastructure of MCF-7 Breast Cancer Cell

Qurrothul Dwi Aini,[1] Anom Bowolaksono,[1] Astari Dwiranti[1]

[1]Cellular and Molecular Mechanisms in Biological Systems (CEMBIOS) Research Group, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, 16424, Indonesia

The mortality rate of breast cancer is high due to the risk of side effects of chemotherapy drugs that can kill healthy body cells.[1] Therefore, natural ingredients are needed as more effective anti-cancer that do not cause side effects.[2] Jojoba (*Simmondsia chinensis* (Link) Schneider) seed oil contains bioactive compounds with anti-cancer properties that can induce cytotoxic activity against HCT 116, MV 3, and MCF-7 cancer cells.[3] However, its effect on the viability and ultrastructure of MCF-7 breast cancer cells is not yet known. This study aims to determine the effect of jojoba seed oil in reducing viability using trypan blue and changing the ultrastructure of MCF-7 cells using a scanning electron microscope (SEM) (Fig. 1). The oil concentrations used were 50, 100, 200, 300, 400, and 500 µg/mL with an incubation time of 72 hours. Statistical analysis showed a significant difference in the percentage of MCF-7 cell viability between the control treatment and 200 µg/mL jojoba seed oil. Observation using SEM shows that 200 µg/mL jojoba seed oil treatment can change the ultrastructure of MCF-7 cells related to shape, lamellipodia, membrane blebbing, and cell membrane holes. Therefore, it is known that jojoba seed oil has an effect in reducing the viability and changing the ultrastructure of MCF-7 cells.

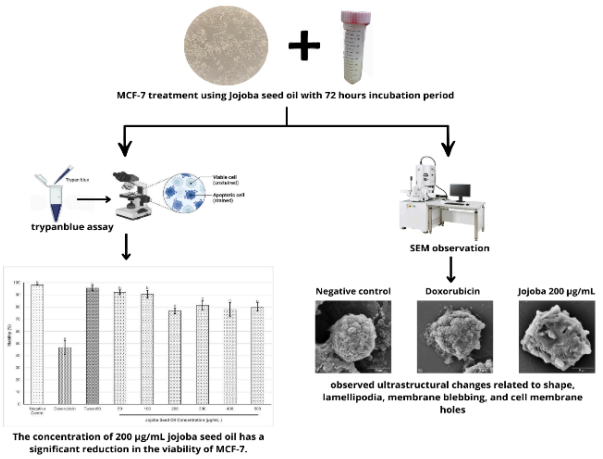
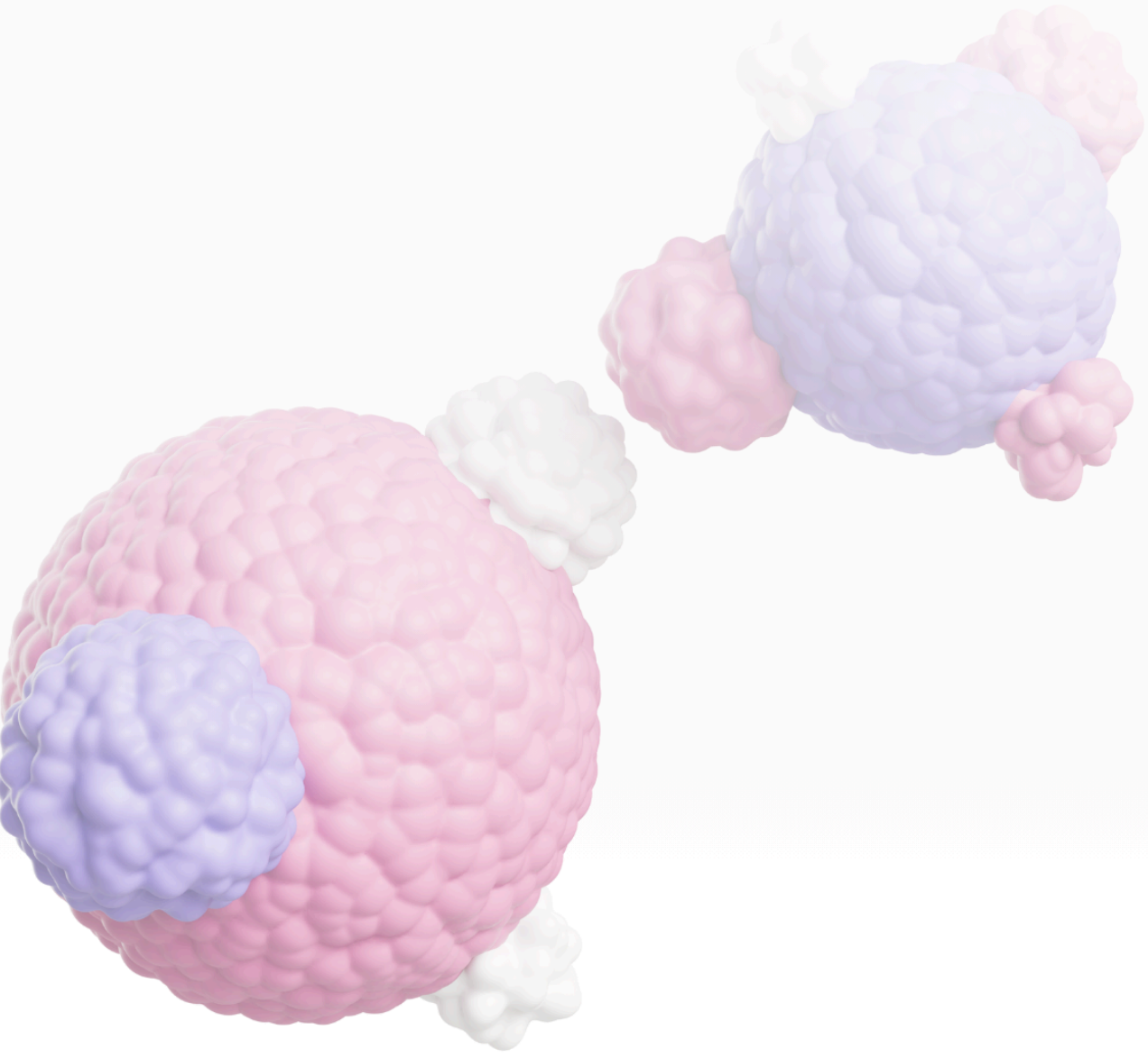



**Fig. 1** Jojoba seed oil effect on the viability and ultrastructure of MCF-7 cell line.

*References*: (1) Fadhillah, A.Q. Aini, Mualifah, Saifudin, A. Bowolaksono & A. Dwiranti. 2022. Effects of *Vetiveria zizanioides* on cytotoxicity of human epithelial cervical cancer cells. *Journal of Hunan University* **49**(2): 329—334; (2) Illian, D.N., I. Hafiz, O. Meila, A.R.H. Utomo, A. Nuryawan, G.A. Siregar & M. Basyuni. 2021. Current status, distribution, and future directions of natural products against colorectal cancer in Indonesia: a systematic review. *Molecules* **26**: 1—18; (3) Al-Qizwini, H., E. Al-Khateeb, N.M. Mhaidat & A. Saleem. 2014. Cytotoxic effects of Jordanian *Simmondsia chinensis* (Link) C.K. schneid on different cancer cell lines. *European Scientific Journal* **10**(24): 182—195.

**Qurrothul D. Aini**
*Student, Universitas Indonesia*

Qurrothul Dwi Aini has just completed her undergraduate degree in the Department of Biology at Universitas Indonesia. She has a strong interest in molecular and cellular biology, focusing on cancer cell culture research. Her undergraduate thesis focuses on the potential of jojoba seed oil as an anticancer agent for breast cancer. During her studies, she was also actively involved in various organizations and community service activities. Her enthusiasm for biomedical science motivates her to contribute and build a career in the field.



# Epidermal and Fibroblast Growth Factor Affect in vitro Culture of Circulating Tumor Cell from Colorectal Cancer in a Concentration Dependent Manner

Rafli Maulana Muhammad[1], Retno Lestari[1], Fadhillah[1], Astari Dwiranti[1], Anom Bowolaksono[1]

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Circulating tumor cells (CTCs) are cancer cells that have detached from their primary site. These cells can be utilized as an approach to determine the appropriate chemotherapy agents because they can be obtained through less invasive methods and share similar characteristics with the original cancer cells.[1] However, one of the challenges is the varied composition of the CTC culture medium used, including components like epidermal growth factor (EGF) and basic-fibroblast growth factor (bFGF).[2] In this study, we aimed to evaluate the effect of EGF and bFGF in CTC cultures isolated using erythrolysis. The cultures were tested with 3 concentrations of EGF and bFGF (0 ng/mL EGF and bFGF, 50 ng/mL EGF and bFGF, and 20 ng/mL EGF and 10 ng/mL bFGF) over 14 days. Their effects on culture viability percentages were analyzed using trypan blue. Cell morphology observed during culture and immunofluorescence were performed. The results showed that EGF and bFGF affect CTC culture viability in a concentration-dependent manner, with the optimal concentration being 20 ng/mL EGF and 10 ng/mL bFGF. Further details will be reported in the symposium.

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**Rafli Maulana Muhammad**
*Student, Universitas Indonesia*

Rafli Maulana Muhammad is a recently graduated with a Bachelor of Science degree in Biology from the Department of Biology, Universitas Indonesia. His research background is focused on cellular and molecular biology, with a particular focus on cancer research. His experience in interning at RIKEN and competing in synthetic biology competition makes him more passionate about biology, particularly in applied biotechnology. His interest include research in biomedical science, synthetic biology, and biotechnology.

# Autophagy-Mediated Protein Degradation in Cancer Cells Induced by Acrolein-Azide [3+2] Cycloaddition

Kana Hasegawa,[1] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

Proteolysis-targeting chimera (PROTAC) have garnered significant attention recently due to their ability to hijack proteolytic pathways in cells. In contrast to conventional small-molecule drugs that primarily inhibit the active site of an enzyme, PROTAC have the potential to target proteins that lack an active site, thereby presenting a promising prospect for expanding the range of drug targets. Nevertheless, unless delivered selectively to the target site in vivo, PROTAC may also act on normal cells, leading to undesirable side effects.

Our laboratory has identified that most cancer cells overproduce acrolein while healthy cells do not.[1] Furthermore, we have demonstrated that adding phenyl azide to cancer cells induces a reaction with acrolein, producing a diazo compound derivative. This diazo compound forms a covalent bond with intracellular molecules and remains inside the cancer cells.[2] In this study, we aimed to selectively degrade cancer cells by utilizing the reaction between the chimeric compound of an autophagy-lysosomal degradation tag linked to phenyl azide with acrolein in the cancer cells (Fig. 1). Synthesis and cell evaluation of the chimeric compounds will be reported in the symposium.

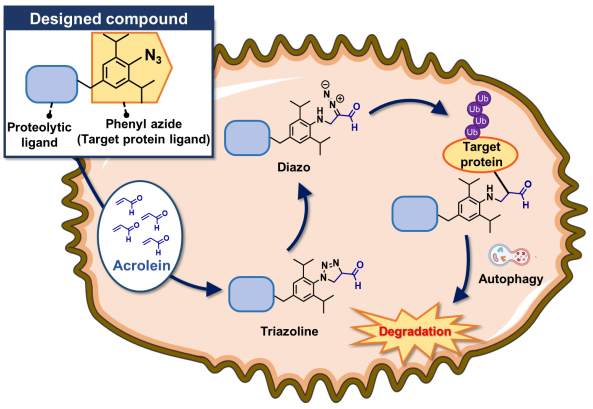


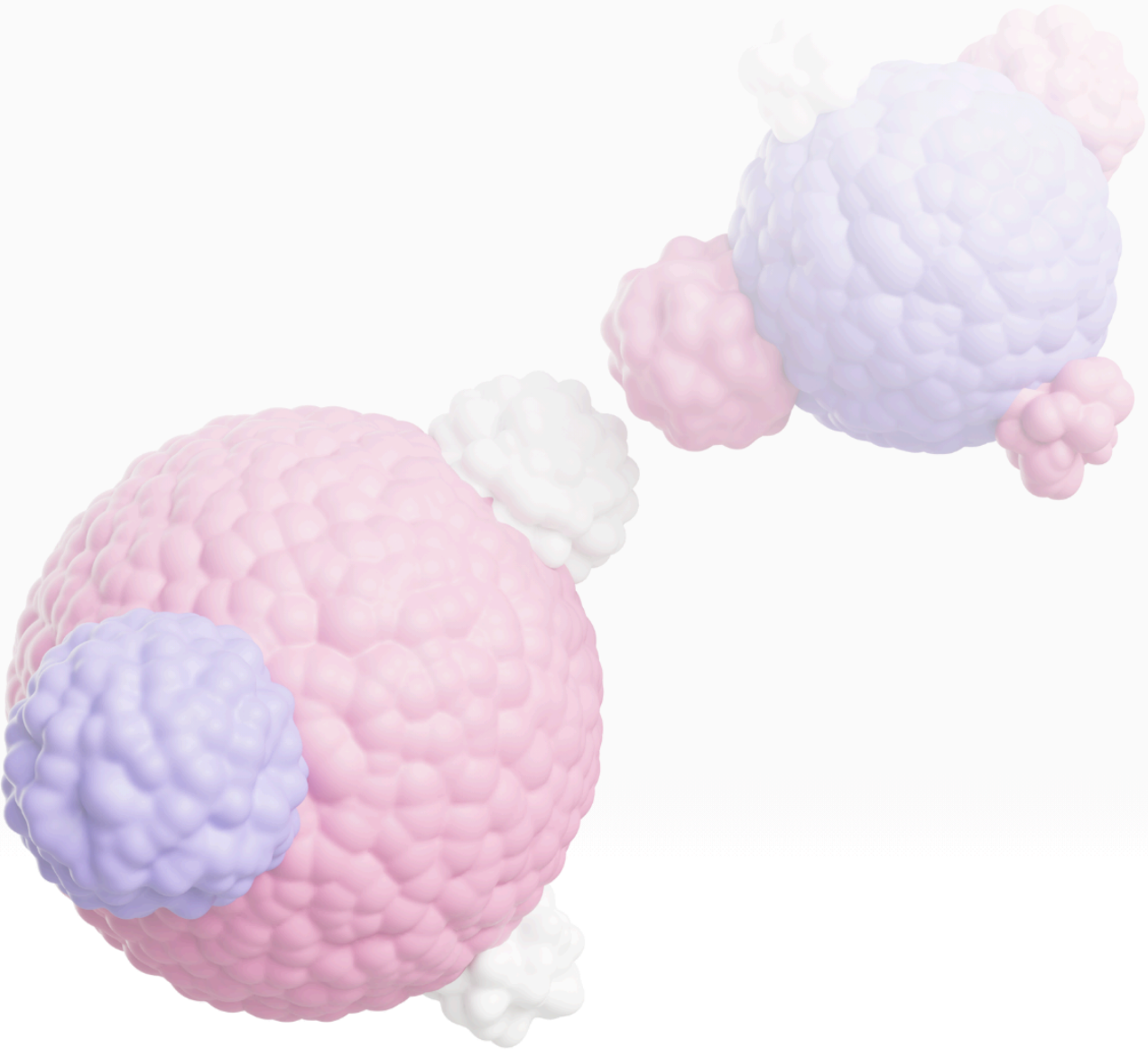

**Fig. 1** Outline of this work

*References*:

1. T. Tanei, A. R. Pradipta, K. Morimoto, M. Fujii, M. Arata, A. Ito, M. Yoshida, E. Saigitbatalova, A. Kurbangalieva, J.-I. Ikeda, E. Morii, S. Noguchi and K. Tanaka, *Adv. Sci.* **2019**, *6*, 1801479.
2. A. R. Pradipta, M. Taichi, I. Nakase, E. Saigitbatalova, A. Kurbangalieva, S. Kitazume, N. Taniguchi and K. Tanaka, *ACS Sens.* **2016**, *1*, 623-632.

**Kana Hasegawa**
Master Student,
Tokyo Institute of Technology

Kana Hasegawa (長谷川 佳奈). Tokyo University of Science (B.Eng. (Chemistry), Faculty of Science Division I, 2023). Current: 2nd Year Student of Master Course. Research field: Organic Synthetic Chemistry, Bioorganic Chemistry. Hobbies and Interests: Tennis



# Therapeutic In Vivo Synthetic Chemistry with Gold Artificial Metalloenzymes for Brain Cancer Treatment

Mori Hara,[1] Yudai Ode,[1] Yasuko Egawa,[2] Hsin-Kai Tseng,[3] Chun-Cheng Lin,[3] Ambara R. Pradipta,[1] Tsung-Che Chang,[2] Katsunori Tanaka[1,2]

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[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan
[3]National Tsing Hua Univ., 101, Section 2, Kuang-Fu Road, Hsinchu 300044, Taiwan R.O.C.

The direct synthesis of drugs at disease sites in vivo, named "Therapeutic In Vivo Synthetic Chemistry" enables drugs to treat diseases without causing side effects in healthy tissues. Previously, we developed biocompatible albumin-based artificial metalloenzymes (ArMs) capable of synthesizing various molecules in blood.[1,2] Moreover, we have demonstrated that glycoalbumins can have diverse organ- or cancer-targeting characteristics by modifying the glycan diversity on the albumin.

In this study, we aim to utilize the glycosylated ArM for treating aggressive brain cancer through the in vivo synthesis of an anticancer drug (Fig. 1). First, we have developed a glucosylated prodrug that can be activated by a gold-based ArM to form a highly toxic drug. Since the prodrug contains glucose, this allows the prodrug to be transported to the brain tumor tissue through glucose transporters. With brain-targeting glycans, we expect that the glycosylated gold-based ArM will accumulate in the brain tumor and that the drug can be synthesized from this prodrug on the brain tumor without causing side effects.

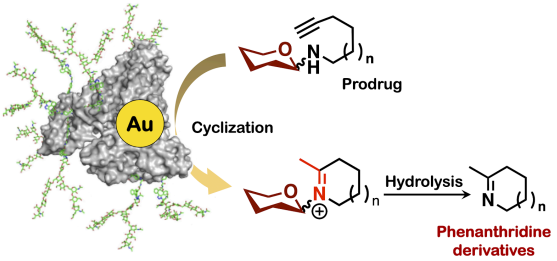


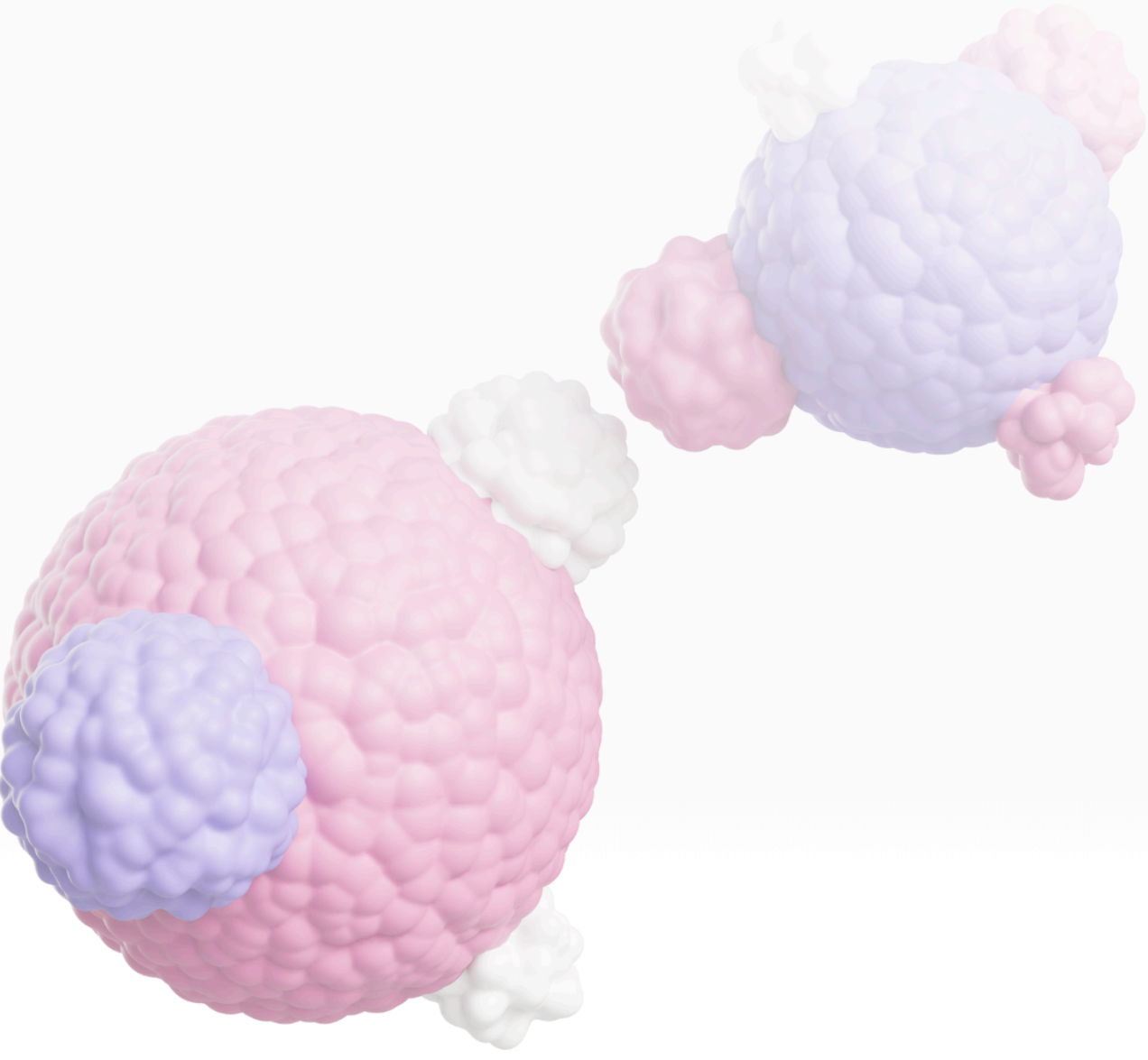

**Fig. SEQ Fig. * ARABIC 1** Strategy of treating brain tumors

*References*:

1. S. Eda, I. Nasibullin, K. Vong, N. Kudo, M. Yoshida, A. Kurbangalieva, K. Tanaka, *Nature Catal*. **2019**, *2*, 780.
2. I. Nasibullin, I. Smirnov, P. Ahmadi, K. Vong, A. Kurbangalieva, K. Tanaka, *Nature Commun*. **2022**, *13*, 39.

**Moeri Hara**
*Master Student,*
*Tokyo Institute of Technology*

Moeri Hara got a bachelor's degree in the Department of Chemical Science and Engineering, Tokyo Institute of Technology in 2023. Afterward, she is studying about organic synthetic chemistry, artificial metalloenzyme, and in vivo synthesis as a master's student at the same university. Her research focuses on developing "therapeutic in vivo synthetic chemistry" strategies for treating brain tumors. In her free time, she enjoys making handmade fashion jewelry.



# Selective Labeling and Functional Analysis of Cancer Cells using Artificial Metalloenzymes

Sawa Inukai,[1] Tsung-Che Chang,[2] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

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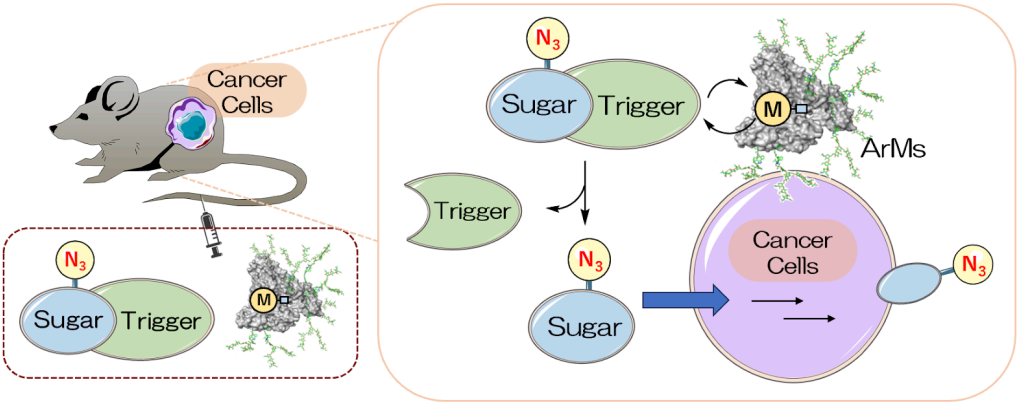
Transition metal catalysts cannot work in vivo because of deactivation by biomolecules such as glutathione. To solve this problem, we previously found that transition metal catalysts can be anchored to hydrophobic pockets in human serum albumin (HSA) to form artificial metalloenzymes (ArMs), thereby protecting their catalytic activity.[1] Furthermore, our research revealed that decorating the surface of HSA with targeting molecules resulted in accumulating HSA in selective cancers or organs in vivo.[2] In addition, many studies showed that the unnatural glycan Ac4ManAz, which has an azido group, can be metabolically incorporated into cells to induce the expression of azido groups on the cell surface.[3] Together with these techniques, we report a strategy of selective labeling cancer cells with azido groups through localized synthesizing Ac4ManAz-like azido sugars at the target site by the tumor-targeting ArMs. The details will be presented at the symposium.




*References*:
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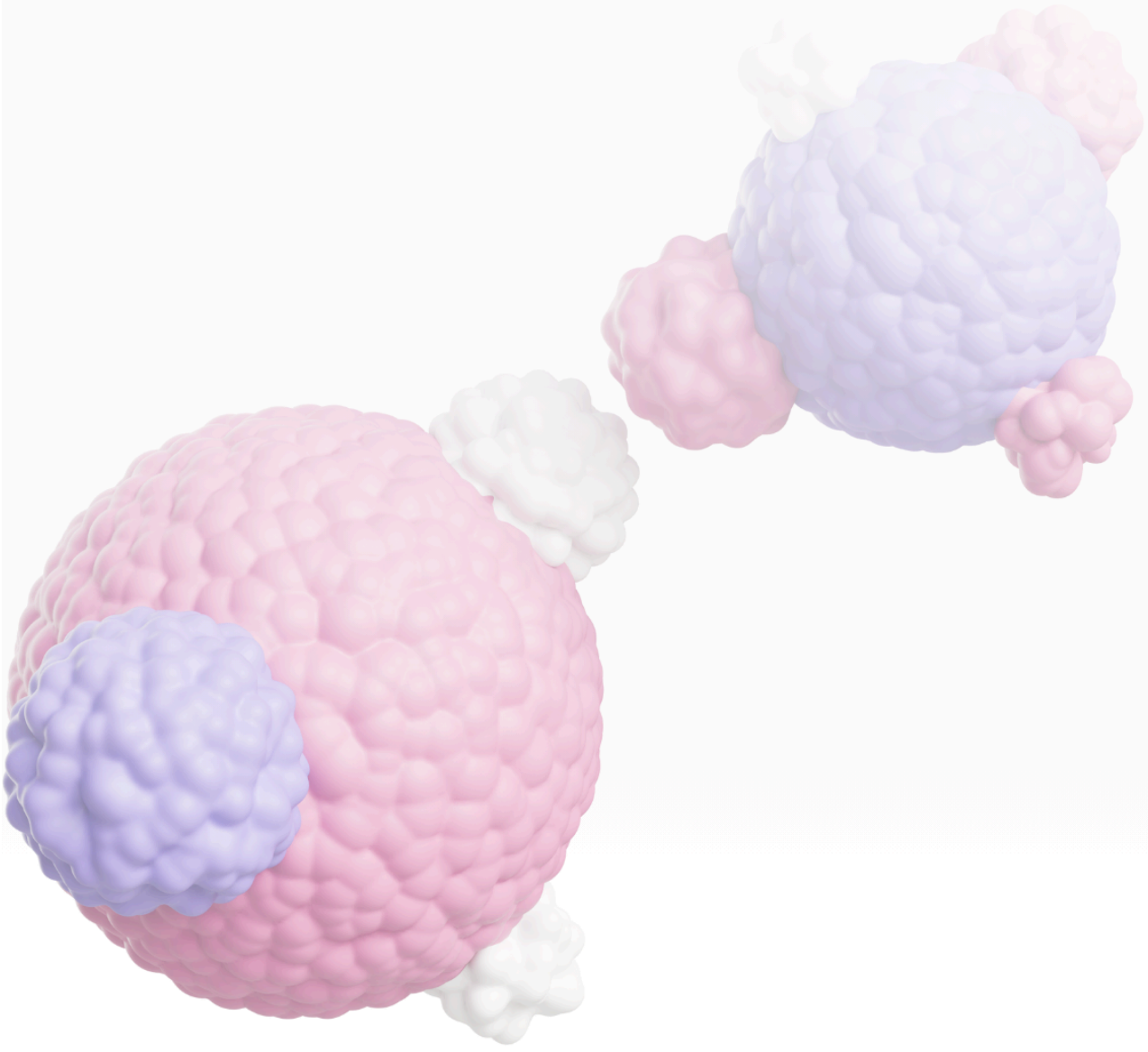
Master Student,
Tokyo Institute of
Technology

Sawa Inukai (犬飼 沙和). Tokyo Institute of Technology (B.Eng. (chemistry), Department of Chemical Science and Engineering, 2023). Current: 1st Year Student of Master Course. Research field: Organic Synthetic Chemistry, Artificial Metalloenzyme, In vivo Synthesis. Hobbies and Interests: Black tea and cooking.



# Treatment of tumor bleeding by therapeutic in vivo ring-opening metathesis polymerization

Yoshito Nakada,[1] Ambara R. Pradipta,[1] Tsung-Che Chang,[2] Katsunori Tanaka[1,2]

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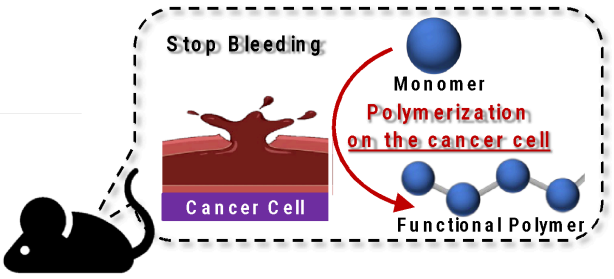
The direct synthesis of drugs in vivo enables drugs to treat diseases without causing side effects in healthy tissues. Transition-metal reactions have been widely explored for uncaging and synthesizing bioactive drugs in biological environments because of their remarkable reactivity. In our previous research, we developed the world's first albumin-based artificial metalloenzyme (ArM) capable of catalyzing various organic reactions in blood. Furthermore, by modifying the surface of albumin with tumor-targeting ligands, we succeeded in delivering ArMs to tumor sites within the body. Using these technologies, we synthesized anticancer drugs on-site in target tumors for treatment in mice.[1,2]

In comparison with small molecules, i.e., drugs, Polymers have recently gained significant attention in the field of medicine; however, their insolubility when administered intravenously will lead to vascular embolism. Typically, introducing functional polymers into the body requires direct administration through laparotomy or endoscopy.

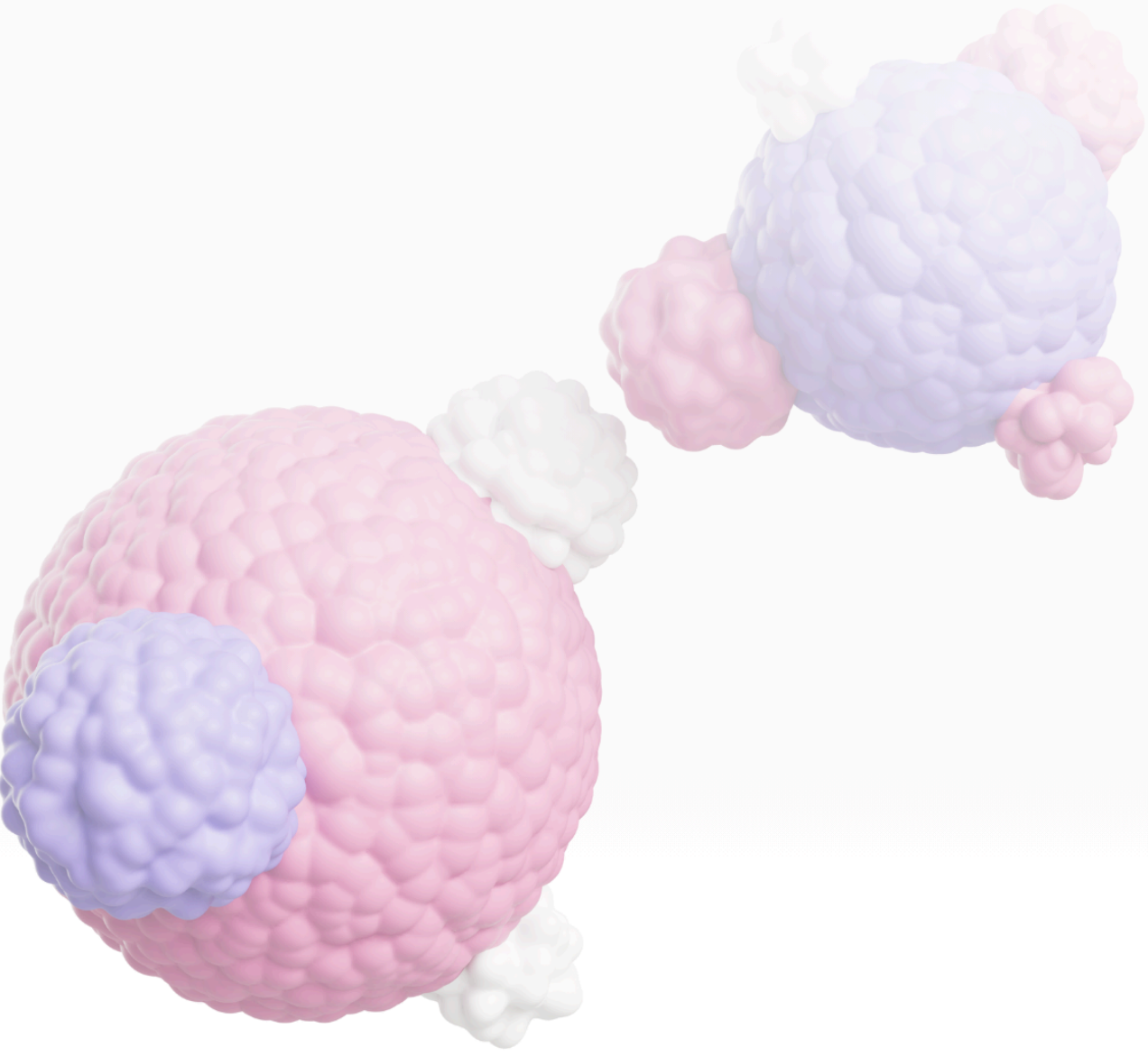
In this study, we aim to synthesize functional polymers at specific locations for treatment in the body, particularly in cancerous tissues. In a preliminary investigation, we successfully catalyzed the synthesis of various types of polymers (MW > $10^5$) from low-molecular-weight monomers in blood via our biocompatible ArMs. This achievement marks the first-ever polymerization reaction catalyzed by a metal catalyst in blood. With this technology, we are proceeding with an innovative hemostasis method where adhesive polymers are synthesized on-site at bleeding and cancer sites (see figure). We expect that this research can create new possibilities for using polymers in medical applications.




1. Eda, S.; Nasibullin, I.; Vong, K.; Kudo, N.; Yoshida, M.; Kubangalieva, A.; and Tanaka, K. *Nature Catal* **2019**, 2, 780.
2. Nasibullin, I.; Yoshioka, H.; Mukaimine, A.; Nakamura, A.; Kusakari, Y.; Chang, T.-C.; Tanaka, K. *Chem. Sci.* **2023**, 14, 11033.

**Yoshito Nakada**
*Master Student,*
*Tokyo Institute of Technology*

Yoshito Nakada. Tokyo Institute of Technology, School of Materials and Chemical Technology, Department of Chemical Science and Engineering (1st year master's degree program). Research fields: Biorthogonal chemistry, Organic synthetic chemistry



# Utilization of Tailor-Made Synthetic Glycoalbumins for Cancer Treatment

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[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

Cancer is caused by various genetic mutations, but in cancers that progress within the patient's body, heterogeneity of genetic mutations reduces the effectiveness of treatment. Currently, there are no effective therapeutic agents available for genetic mutations even when diagnosed by multi-gene panel testing. In addition, current targeted delivery systems that can be commonly used at the individual level for cancers with different gene mutations are limited. To address this problem, tailor-made therapies optimized for cancer are desired.

Cluster formation by different types of natural glycan molecules on cell surfaces results in distinct "glycan patterns". These glycan patterns facilitate selective cell recognition, i.e., glycan pattern recognition, which plays important roles in several biological processes.[1] Previously, we have developed a method called RIKEN click reaction, which allows for the efficient construction of various types of glycans on human serum albumin. These glycoalbumins have capability to selectively bind to various cancer cells by the "pattern" of matching with multiple glycans.

In this study, we synthesized hundreds of kinds of glycoalbumins with diverse glycan patterns and screened for optimal glycoalbumins for cancers with various gene mutations. Then, the obtained glycoalbumins will be used as a delivery system to activate drugs for treatment. Ultimately, based on this glycan and lectin pattern recognition, we will establish a general-purpose precision cancer recognition platform, which will be deployed to Tailor-made cancer treatment to each patient's cancer. In this presentation, we will report on the background of these efforts.

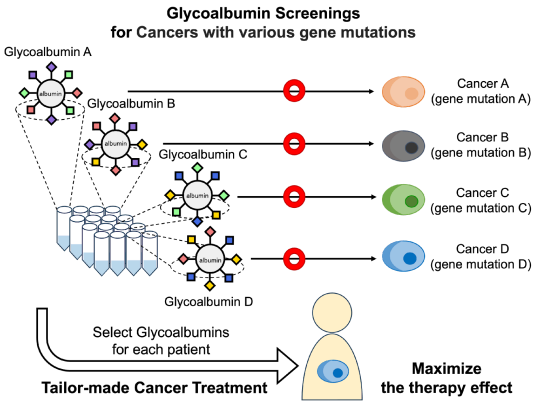
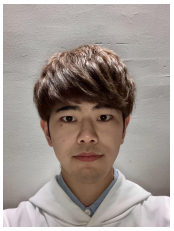


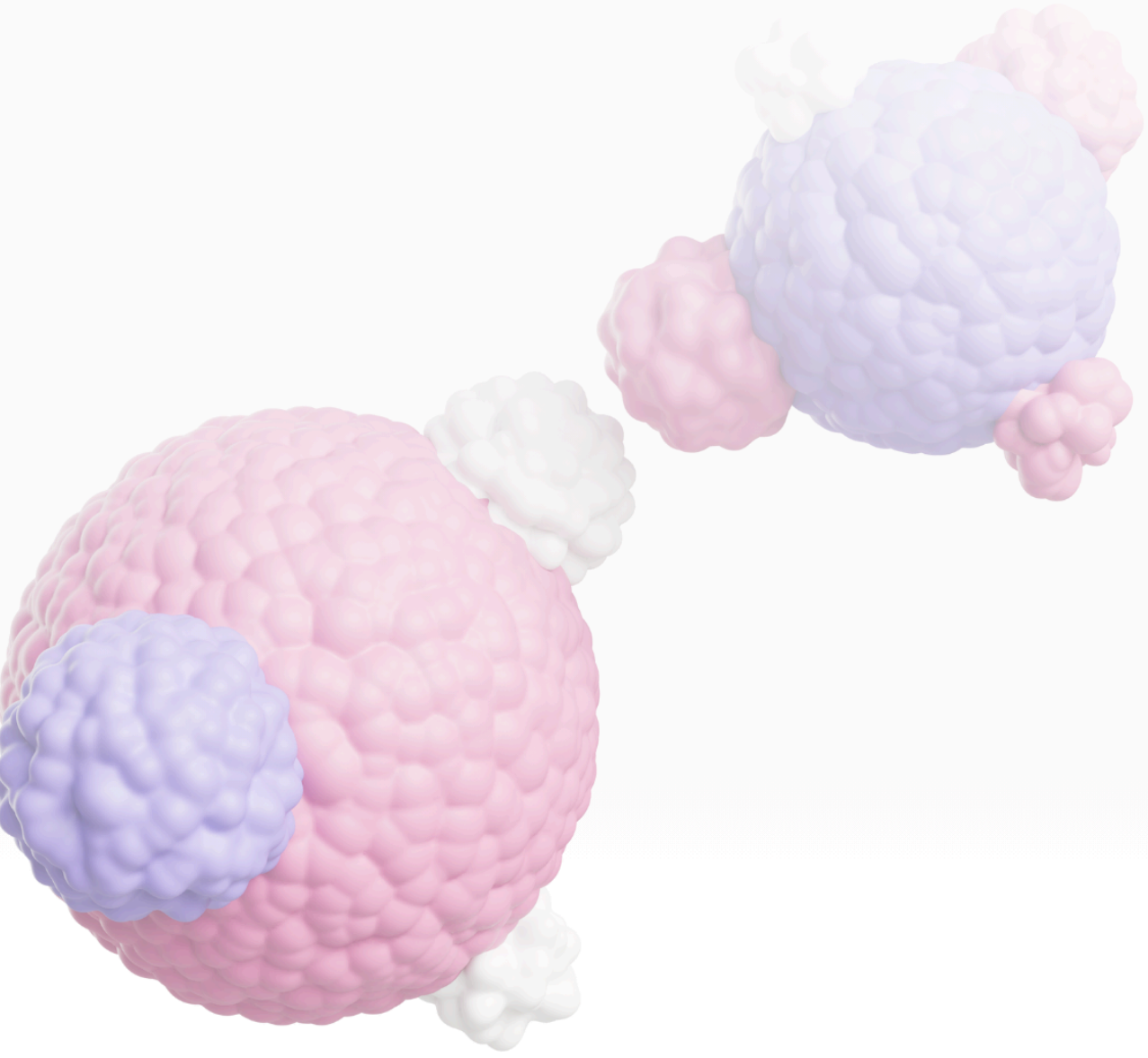

**Fig.1** Glycoalbumin Screening toward tailor-made cancer treatment.

*References*: (1) I. Smirnov, R. Sibgatullina, S. Urano, T. Tahara, P. Ahmadi, Y. Watanabe, A. R. Pradipta, A. Kurbangalieva, and K. Tanaka, *Small* **2020**, 16, e2004831.



**Akito Nunome**,
*Master Student,*
*Tokyo Institute of Technology*

Akito Nunome, Tokyo Institute of Technology, School of Materials and Chemical Technology, Department of Chemical Science and Engineering (1st year Student of Master Course). Research field: Organic Synthetic Chemistry, Glycan Chemistry.
Hobbies and Interests: Photography and Travel.



# Exploiting the Diels-Alder Reaction with Endogenous Acrolein for Cancer Treatment

Yuki Masaki,[1] Kazuki Terashima,[1] Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

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In our laboratory, we have been conducting research on cancer diagnosis and treatment. We are converting metabolites from living organisms into drugs that can be used in the body. During our research, we discovered that acrolein, an unsaturated aldehyde, is generated at high levels in cancer cells. We have also developed a prodrug method using aryl azides, which selectively undergo [3+2] cyclization with acrolein and have shown effective cancer therapy without side effects in model mice. We plan to further explore the potential applications of acrolein reactions in in vivo synthetic chemistry. In this study, we aim to use the Diels-Alder (DA) reaction of endogenous acrolein to treat cancer (Fig. 1).

In this study, we successfully conducted the DA reaction within cancer cells by using endogenous acrolein. We observed the reaction products using LC-MS. Furthermore, we investigated further applications of this reaction for cancer treatment.

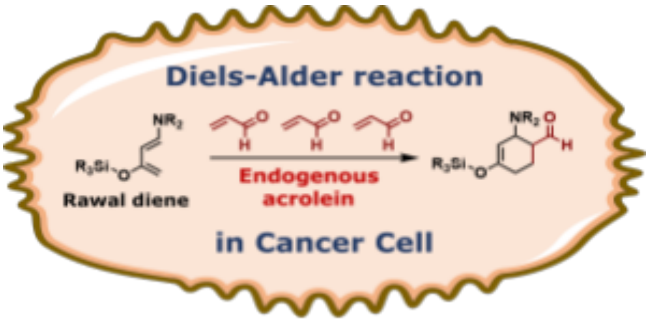


**Fig. SEQ Figure * ARABIC 1** Diels-Alder reaction of acrolein for cancer treatment

*References*:

1) T. Tanei, A. R. Pradipta, K. Morimoto, M. Fujii, M. Arata, A. Ito, M. Yoshida, E. Saigitbatalova, A. Kurbangalieva, J. -I. Ikeda, E. Morii, S. Noguchi, K. Tanaka, *Adv. Sci.* **2019**, *6*, 1801479.
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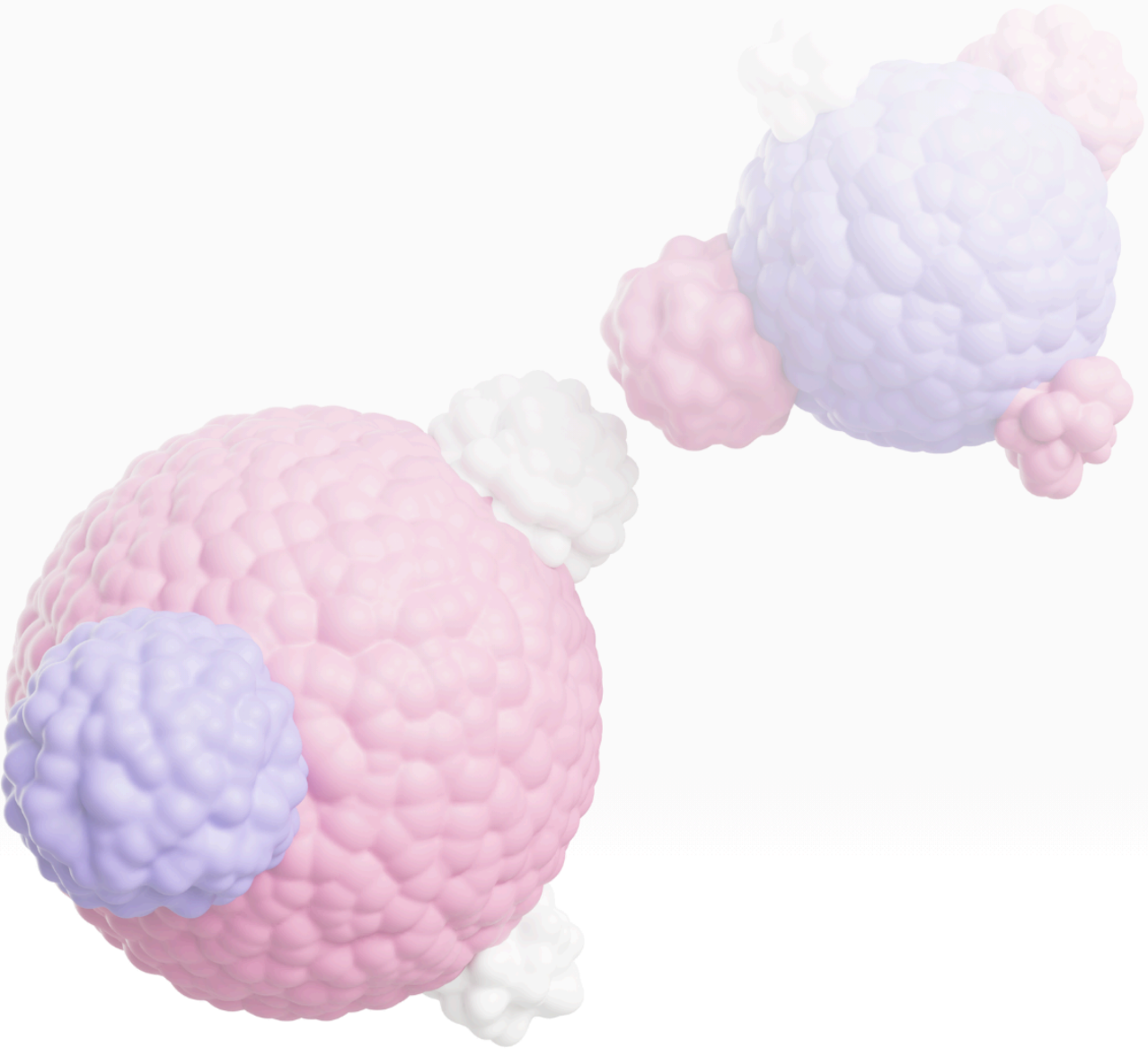
3) T. Kasahara, T.-C. Chang, H. Yoshioka, S. Urano, Y. Egawa, M. Inoue, T. Tahara, K. Morimoto, A. R. Pradipta K. Tanaka, *Chem. Sci.* **2024**, *15*, 9566.

**Yuki Masaki**
*Master Student, Tokyo Institute of Technology*

Yuki Masaki completed his bachelor's studies in the Department of Chemical Science and Engineering at the Tokyo Institute of Technology, in March 2024. He has been in his current position since April 2024. His expertise lies in bioorganic chemistry, organic synthesis chemistry. His research focuses on developing advanced diagnostic and therapeutic methods by converting metabolites from living organisms into diagnostic and therapeutic agents through organic synthesis chemistry. In his free time, he enjoys eating sweet foods.



# Selective Activation of PROTACs in Cancer Cells via Metathesis Reaction using Artificial Metalloenzymes

Yuta Shimura,[1] Masayuki Kawai,[1] Hiromasa Yoshioka,[2]
Ambara R. Pradipta,[1] Katsunori Tanaka[1,2]

[1]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
[2]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

Proteolysis-targeting chimeras (PROTACs) are molecules composed of a ligand that binds to an E3 ligase and another ligand that binds to a target protein, conjugated together by a linker. These molecules have garnered significant attention recently for their ability to selectively degrade specific proteins (Fig. 1a). In this study, we use PROTACs to selectively degrade the cholesterol-synthesizing enzyme SQLE, which is highly expressed in cancer cells.

However, a challenge with conventional PROTACs is their difficulty selectively degrading target proteins only within specific cancer cells. To address this issue, this study aims to utilize an artificial metalloenzyme developed previously in our laboratory, capable of selectively targeting cancer cells. This approach involves converting PROTAC precursors near cancer cells to induce the degradation of SQLE (Fig. 1b). Additionally, since the linker length is crucial for PROTAC activity, we synthesized PROTAC derivative with different linker lengths to explore the optimal structure. Herein, we report the synthesis of PROTAC and its activity evaluation. The details will be reported at the symposium.

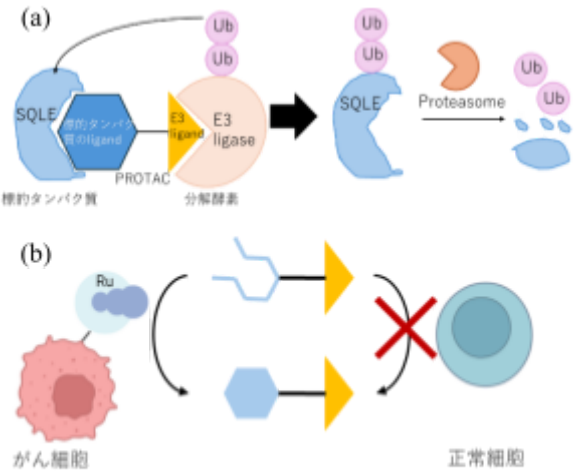



**Fig. 1** Research outline.

**Yuta Shimura**
*Undergraduate Student,*
*Tokyo Institute of Technology*

Yuta Shimura (志村 優太). Tokyo Institute of Technology. Undergraduate Student, 4th year. Research Field: Bioorganic Chemistry.

# Synthesis and enzymatic degradation of D-arabinan fragments from anticancer immunostimulating mycobacterial cell wall skeleton

Akihiro Ishiwata,[1] Katsunori Tanaka[1,2] and Yukishige Ito[1,3]

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[3]Graduate School of Science, Osaka University, 1-1 Machikaneyama, Toyonaka, Osaka 560-0043, Japan

Arabinan is a polysaccharide component composed of D-arabinofuranoside (Ara*f*) in mycobacterial cell wall as mycolyl arabinogalactan-peptidoglycan complex and lipoarabinomannan. The cell wall skeleton has been shown to be a cancer immunostimulating agent. The branched arabinan structure contains α-(1→5), α-(1→3) and β-(1→2) linkages, and connects to mycolic acid. Multidrug-resistant bacteria are a major problem of *Mycobacterium tuberculosis*, and the glycan biosynthesis is regarded as an important target for new antibacterial agents. Exo- and endo-type hydrolases in glycoside hydrolase (GH) family 116, 172 and 183 from *Microbacterium arabinogalactanolyticum*, that degrades the arabinan, respectively,[1] which were also interested as a new target candidate for anti-tuberculosis agent.

Synthetic study of unexplored complex structure had been carried out by stereoselective synthesis of 1,2-*cis*-β-arabinofuranosides,[2] and convergent strategy for the synthesis of highly branched arabinan structure (Fig. 1).[3] The probes with a characteristic motif structure have been prepared to analyze the reaction mechanisms of enzymes and the substrate specificity of the GH183 enzyme.[1]

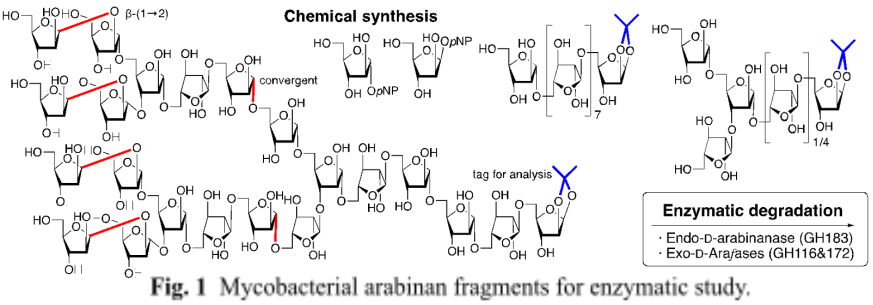
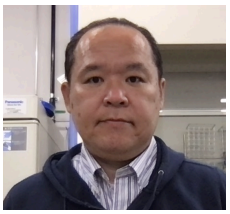


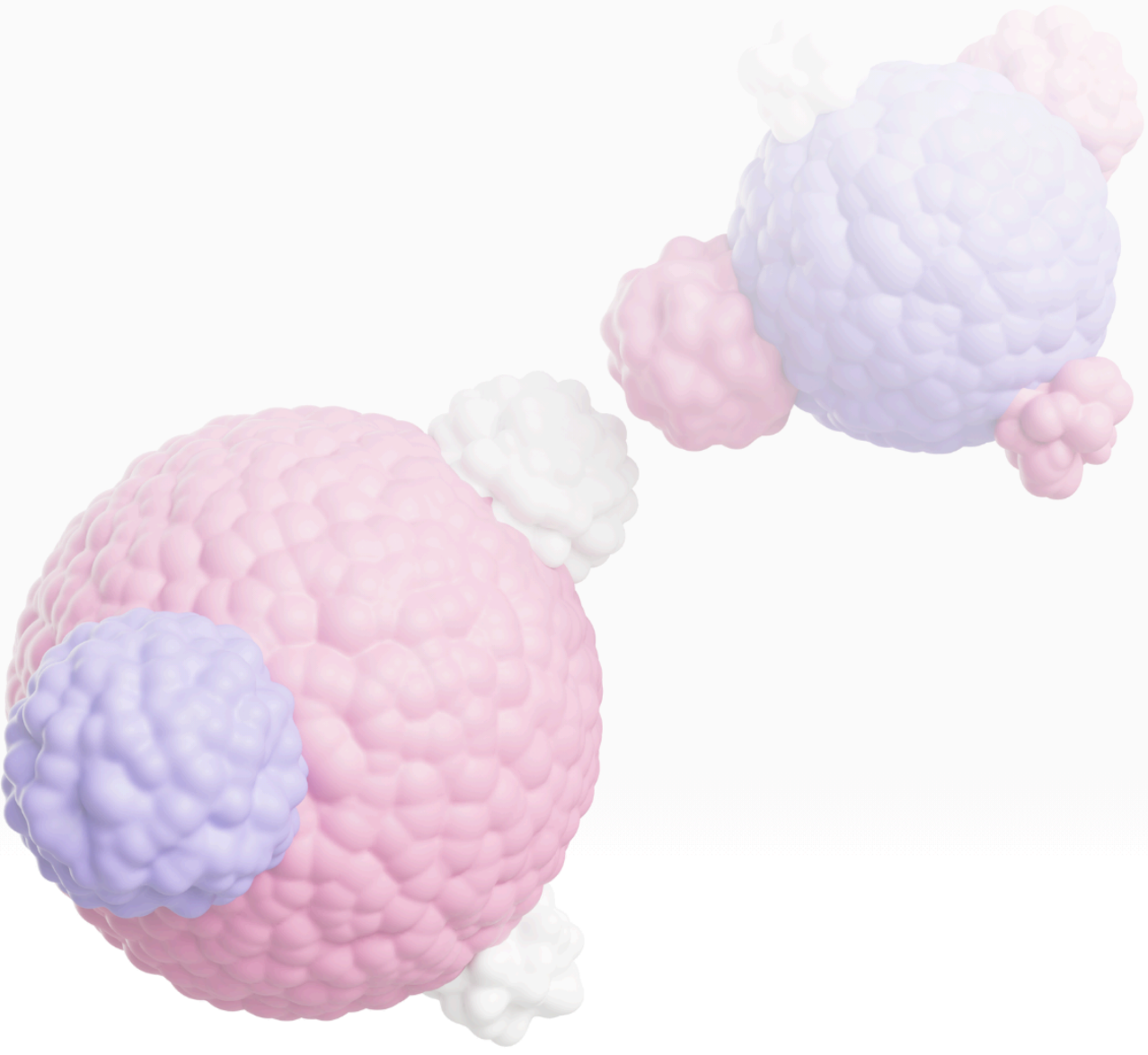

**Fig. 1** Mycobacterial arabinan fragments for enzymatic study.

*References*:
1. Shimokawa, M. et al. *Nat. Commun.* **2023**, *14*, 5803.
2. Ishiwata, A., Ito, Y. *JACS* **2011**, *133*, 2275.
3. Ishiwata, A. et al. *Eur. J. Org. Chem.* **2008**, *25*, 4250; Xiao, Q. et al. *ACS Omega* **2024**, *9*, 11969.



**Akihiro Ishiwata**
*Senior Research Scientist, RIKEN Cluster for Pioneering Research*

Dr. Akihiro Ishiwata obtained his Ph.D. in 1998 from Tohoku University under supervision of Professor Masahiro Hirama. After three years post-doc training at Sagami Chemical Research Center and Wayne State University under direction of Dr. Shiro Terashima and Professor Shahriar Mobashery, respectively, he moved to RIKEN as a researcher in Synthetic Cellular Chemistry laboratory directed by Dr. Yukishige Ito in 2001. Now he is a senior research scientist at RIKEN・Cluster for Pioneering Research. His main research interests cover glycochemistry and glycoconjugate chemistry.



# Synthesis of Tricyclic Diterpenoids Using Artificial Metalloenzyme Toward Cancer Therapy

Riichi Hashimoto,[1] Tsung-Che Chang,[1] Katsunori Tanaka[1,2]

[1]Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-1098, Japan

[2]Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan

In cancer therapy, the prodrug strategy, which synthesizes an active drug from an inactive form (prodrug) only near cancer cells, is one of the most popular solutions to side effects. Until now, we have established an artificial metalloenzyme that enables the activation of the above-mentioned prodrugs.[1] In this study, we aimed to develop a new method of prodrug activation while generating a fluorescent molecule using the artificial metalloenzyme. This method has the potential to enable real-time monitoring of prodrug activation.

We found that Au-catalyzed hydroamination[2] cleaved the acyl group of the prodrug simultaneously with the generation of the fluorescent molecule (Fig. 1). This reaction also proceeded by albumin-Au complex as an artificial metalloenzyme in PBS buffer. In the poster, we will present the details of our findings.

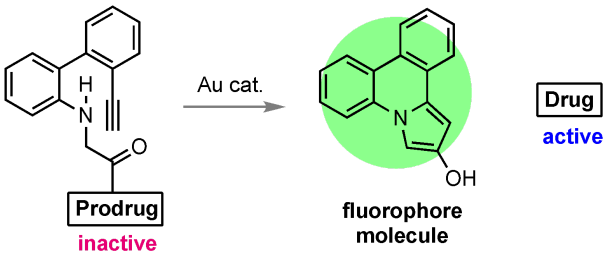



**Fig. 1** Prodrug activation by artificial metalloenzyme accompanied by the formation of fluorescent molecules.

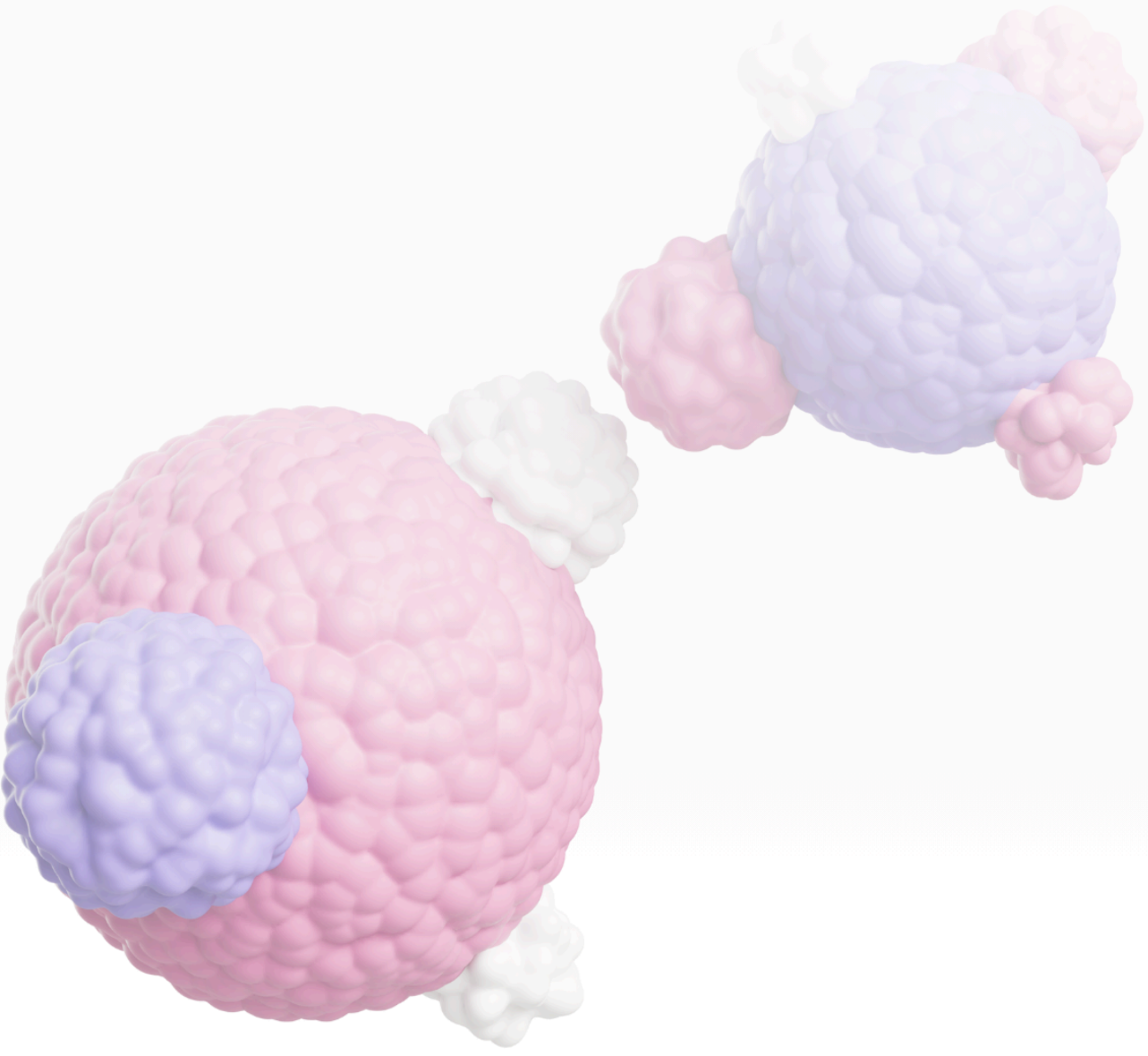
*References*:

1. Eda, S., Nasibulin, I., Vong, K., Kudo, N., Yoshida, M., Kurbangalieva, A., Tanaka, K. *Nature Catal.* **2019**, *2*, 780.
2. Chang, T.-C., Vong, K., Yamamoto, T., Tanaka, K. *et al.*, *Angew. Chem. Int. Ed.* **2021**, *60*, 12446.

**Riichi Hashimoto**

*Postdoctoral Researcher,*
RIKEN Cluster for
Pioneering Research

Riichi Hashimoto completed his doctoral studies in the Department of Pharmaceutical Science at the Graduate School of Pharmacy, Keio University in 2023. Afterward, he has been in his current position since April 2023. His expertise lies in organic synthesis chemistry, natural product chemistry and bioorganic chemistry. His research focuses on developing new reaction that can be applied to treatments or diagnosis. In his free time, he enjoys playing badminton and tennis.

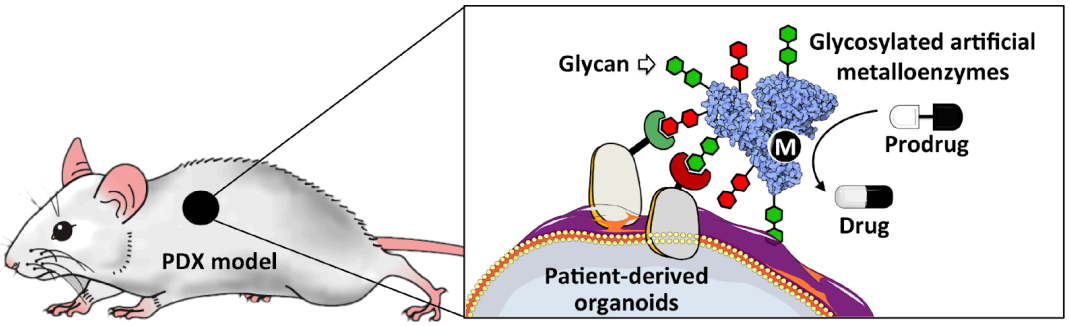


# Cancer Treatment in PDO and PDX Models Using Therapeutic *In Vivo* Synthetic Chemistry

Akiko Nakamura,[1] Yuriko Kusakari,[1] Tsung-Che Chang,[1] and Katsunori Tanaka[1,2]

[1] Biofunctional Synthetic Chemistry Laboratory, Cluster for Pioneering Research, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan
[2] Department of Chemical Science and Engineering, School of Materials and Chemical Technology, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan

The direct synthesis of drugs at disease sites *in vivo*, named "*Therapeutic In Vivo Synthetic Chemistry*"[1] enables drugs to treat diseases without causing side effects in healthy tissues. One of the significant components that drives cell-to-cell interactions is glycan recognition with lectins.[2] Since most malignant cells have altered their lectin patterns compared to healthy cells, this represents a potential cancer-targeting mechanism. Here, we have identified a glycoalbumin that can effectively target patient-derived tumor organoids (PDO). By adapting the targeting glycoalbumin to become a glycosylated artificial metalloenzyme (GArM), *in vitro* and *in vivo* results showed that our "*Therapeutic In Vivo Synthetic Chemistry*" could induce a significant inhibition of cancer cell growth in PDO and patient-derived xenograft (PDX) model.

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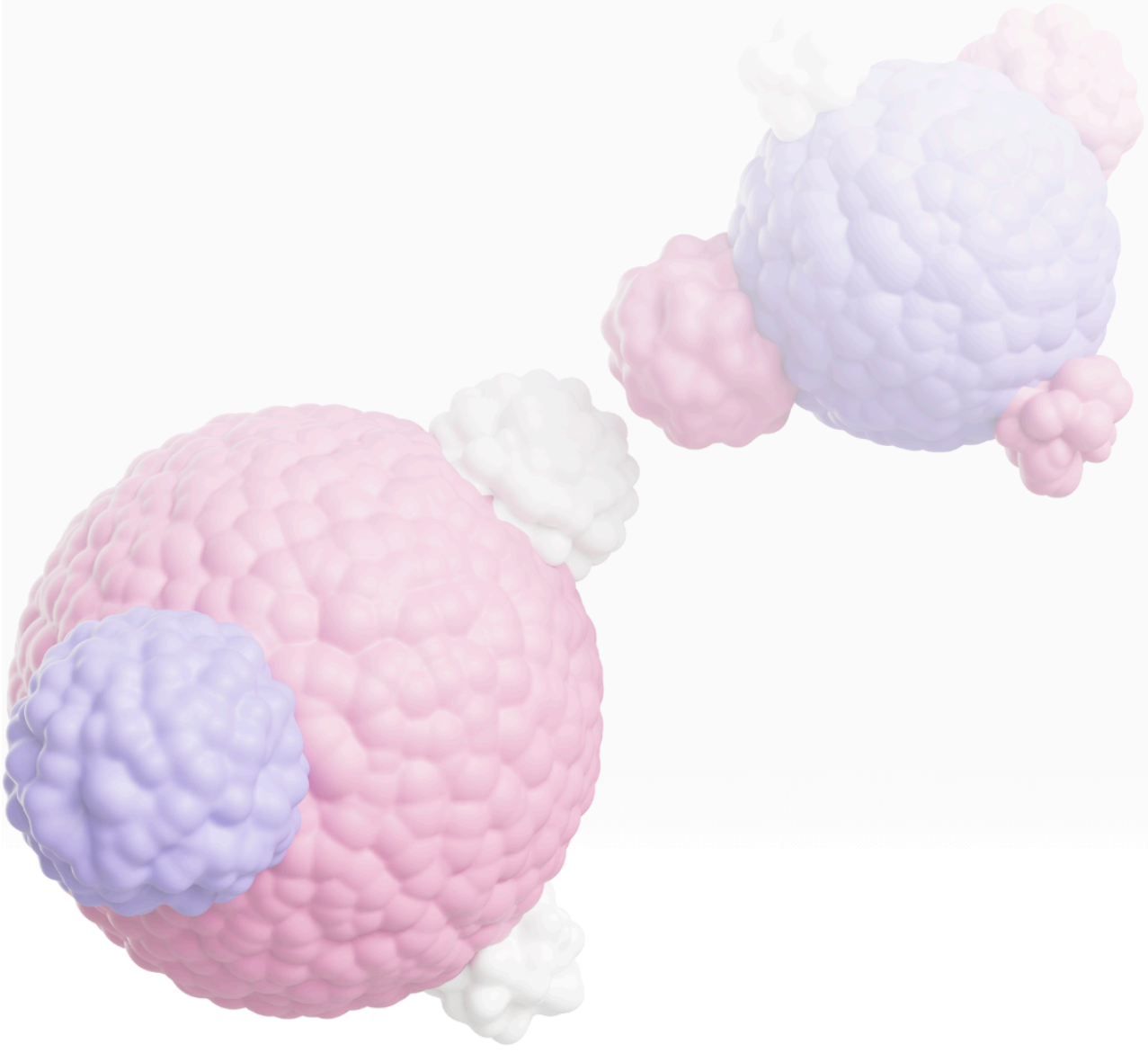
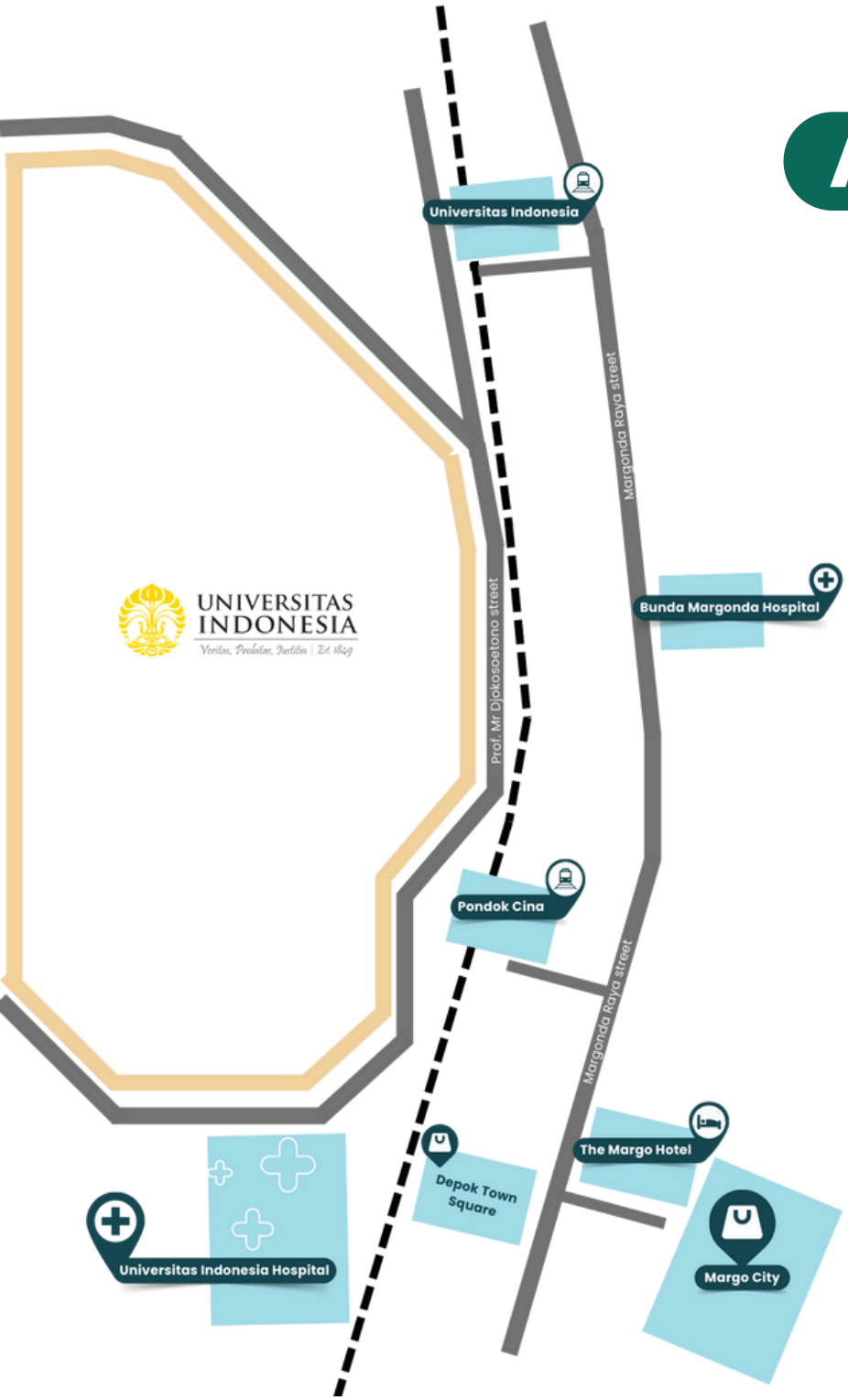
2. Nasibullin, I.; Smirnov, I.; Ahmadi, P.; Vong, K.; Kurbangalieva, A.; Tanaka, K. *Nature Commun.* **2022**, *13*, 39.
3. Nasibullin, I.; Yoshioka, H.; Mukaimine, A.; Nakamura, A.; Kusakari, Y.; Chang, T.-C.; Tanaka, K. *Chem. Sci.* **2023**, *14*, 11033.
4. Vong, K.; Yamamoto, T.; Tanaka, K. *Small,* **2020**, *16*, 1906890

**Akiko Nakamura**
*Technical Staff,*
*RIKEN Cluster for*
*Pioneering Research*

Akiko Nakamura. Chiba University (B.S., 2006). Bioengineering Laboratory (2019). Biofunctional Synthetic Chemistry Laboratory, RIKEN (2021).
[Field of research] Biochemistry



# MAP AREA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