

# VOLUME 13 · FEBRUARY 2021

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HIROSHIMA UNIVERSITY

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# CAMPUS PHOTOS WINTER



# **HIROSHIMA UNIVERSITY**

Embodying its founding principle of "a single unified university, free and pursuing peace," Hiroshima University is one of the largest comprehensive research universities in Japan. Today, HU is making steady progress as a global university, taking on worldwide challenges and strengthening its global educational network by signing international exchange agreements with universities around the world and opening overseas bases at strategic locations.



HIROSHIMA UNIVERSITY

#### **HIROSHIMA UNIVERSITY UPDATE**

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Morning at Hiroshima University Satake Memorial Hall, Higashi–Hiroshima Campus



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### HIROSHIMA UNIVERSITY ESTABLISHES BEIJING BRANCH OF ITS MORITO INSTITUTE OF GLOBAL HIGHER EDUCATION

On December 1, 2020, Hiroshima University (HU) concluded a memorandum of understanding with Capital Normal University (CNU) on establishing HU's Morito Institute of Global Higher Education Beijing Branch. HU and CNU also concluded an international exchange agreement in 2002, and in the same year established the Beijing Research Center, HU's first overseas base, where educational and research exchanges are ongoing.

The signing ceremony was held online at HU's Kasumi Campus with President Mitsuo Ochi, Executive Vice President Toshiyuki Sato, and Executive Vice President Satoshi Watanabe attending from HU. From CNU, President Meng Fanhua, Director Han Mei of International Cooperation and Exchange, Vice Director Lu Qiaomei of International Cooperation and Exchange, and Professor Li Junyang were in attendance. The memorandum of understanding was signed by both President Ochi and President Meng.

President Ochi expressed his hopes for the future, saying, "I hope that the establishment of the Morito Institute of Global Higher Education in Beijing will deepen the cooperation between Capital Normal University and our own university, further developing both universities."

President Meng also commented, "Our universities have a history of exchange for more than 20 years. Despite COVID-19 currently hindering the exchange between the two universities, I would like to work hand-in-hand to create a new cooperative relationship."

Preparations to build HU's Morito Institute of Global Higher Education Beijing Branch within CNU are underway, aiming to start teaching in September 2021. Once established, the school will provide education for students of CNU and other Chinese students interested in improving their practical Japanese language skills and understanding of Japanese culture.

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I hope that the establishment of the Morito Institute of Global Higher Education in Beijing will deepen the cooperation between Capital Normal University and our own university, further developing both universities.



### HU SIGNS 5G, SMART CITY DEVELOPMENT DEAL

On January 26, 2021, HU, Higashihiroshima City and Sumitomo Corporation signed an agreement to achieve Society 5.0 and develop a 5G-ready smart city in Higashihiroshima City and surrounding areas.

A new industry-academiagovernment cooperation model for regional revitalization The purpose of the agreement is to contribute to the world and the local community by promoting the establishment of an environment for innovation and academic research, developing human resources, and fostering industrygovernment-academia collaboration on an international scale.

Intending to realize the Sustainable Development Goals (SDGs) and Society 5.0, Hiroshima University promotes collaboration with Arizona State University in the United States and local authorities in the region, with a vision of international expansion. This agreement will accelerate this goal and make HU a world-class research and education institution adapted to the new post-coronavirus era.

Sumitomo Corporation will set up a "Local 5G" open laboratory in the newly constructed International Exchange Center to work on digital transformation within HU. The lab will promote joint research on the use of 5G with the university and the private sectors, utilize the data on movement and activities within the university, and conduct experiments on light mobility, aiming to expand the application of 5G beyond the campus.



### HU PROFESSOR HONORED AS ONE OF WORLD'S 100 OUTSTANDING WOMEN NURSES AND MIDWIVES



HU Professor Yoko Shimpuku conducts fieldwork in Tanzania to improve maternal and child health conditions

The International Year of the Nurse and the Midwife culminated in 2020 with a celebration of the achievements and societal contributions of 100 exceptional women nurses and midwives worldwide – among them Hiroshima University Professor Yoko Shimpuku who was the sole awardee from Japan.

The 100 Outstanding Women Nurses and Midwives award features the accomplishments of nurse and midwife leaders from 43 countries while putting the spotlight on the courageous work millions of other women in the field are doing, especially as the world faces a raging pandemic. The award was made possible through the partnership of the World Health Organization (WHO), United Nations Population Fund (UNFPA), Nursing Now, International Council of Nurses (ICN), International Confederation of Midwives (ICM), and Women in Global Health (WGH).

#### Training future midwifery leaders

A midwifery expert and academic, Shimpuku is actively involved in research, skills development, and policy work at a national and global level. She is deeply engaged in maternal and child health research in Tanzania, where her focus is on improving the quality of antenatal care and midwifery education. The establishment of one of the first midwifery Master's programs in Tanzania is among Shimpuku's most notable accomplishments.

At a national level in Japan, Shimpuku has devoted herself to educating nurses and midwives with wide global experiences and perspectives as a professor at HU's Graduate School of Biomedical and Health Sciences. She also holds leadership roles in various societies for young scientists as an executive committee member of the Global Young Academy and vicechair of the Young Academy Japan.

She had presented at numerous international conferences and meetings including the 2019 UN International Day of Women and Girls in Science Assembly and the G7 Academy Meeting and reported to the Japanese prime minister as part of her science diplomacy work.

Her latest undertaking was the development of an educational smartphone app that provides midwives life-saving information based on WHO guidelines.

"Through these activities and many more, Professor Shimpuku has had a highly positive impact on the global health ecosystem, with further prominent examples of this impact including reporting her work to Japan's Prime Minister, providing a lecture to HRH Princess Akishino of Japan, her speech at the United Nations' 5th International Day of Women and Girls in Science, and her work as a member of the Science Council of Japan's Gender and Diversity and Gender Equal Participation Committees," her profile on the website dedicated to the International Year of the Nurse and the Midwife said.

### FORMER HU INTERNATIONAL STUDENT RECEIVES NATIONAL DECORATION

On November 3, 2020, Dr. Andi Husni Tanra — a former international student at HU — was awarded the Order of the Rising Sun, Gold Rays with Neck Ribbon at the 2020 Autumn Conferment of Decorations on Foreign Nationals for his contribution to enhancing the academic exchange and friendship between Japan and Indonesia.

After graduating from the Faculty of Medicine, Hasanuddin University in Indonesia, Tanra studied at HU's Graduate School of Medicine from 1976 to 1981, during this time he earned his doctor of medicine. He is currently a professor emeritus of Hasanuddin University and also serving as the President of the Indonesian branch of the Association of Medical Doctors of Asia (AMDA).

Dr. Tanra has made significant contributions towards the improvement of Indonesian medical standards. In the event of earthquakes and tsunamis, he actively devoted himself to humanitarian aid activities. Also, he has made great contributions for years to promote friendship between Japan and Indonesia as the chairperson of the South Sulawesi office of the Association of Indonesian Alumni from Japan (PERSADA), by giving guidance to Indonesian students studying in Japan while introducing Japanese culture to Indonesian people. The Order of the Rising Sun is a decoration conferred by the Japanese government to those who have made outstanding contributions to promote friendly relations and mutual understanding with Japan.



In February 2016, at the Hiroshima University International Exchange Ambassador Certificate Award Ceremony (Center left: Dr. Andi Husni Tanra, Center right: President Ochi)

### PRESERVING A-BOMB VICTIMS' RECORDS FOR FUTURE GENERATIONS

#### Crowdfunding campaign: Specimen Database Project

In 1945, large numbers of pathology specimens and other materials from A-bomb victims had been collected by the United States. The materials were returned to Japan in 1973. Those belonging to the victims of the Hiroshima atomic bombing are now stored at Hiroshima University's Research Institute for Radiation Biology and Medicine (RIRBM).

A lot of research has been conducted in RIRBM using these samples from A-bomb victims. The tissue specimens, however, have deteriorated over time, and the world is on the verge of losing these valuable resources.

Among the glass slides containing internal organ or bone marrow samples returned from the US, about 4,000 are from 135 people autopsied by the end of 1945. The materials, especially those obtained within just a few months after the atomic bombing, are unique and of great value. To keep the images available for research and accessible to the public, HU has launched a project to digitize the A-bomb victim's glass slide specimens.

HU tried raising funds for the project through a crowdfunding campaign called "Preserving A-Bomb Victims' Records for Future Generations: Specimen Database Project." The campaign ran from July 29 to September 30, 2020, gathering a total of JPY 4.5 million in contributions from over 270 supporters. HU sincerely thanks all the contributors for their warm support.

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The project to digitize the glass slide specimens of A-Bomb Victims has just started, and we are going to report the progress of the project from time to time

> Assistant Professor Sayaka Sugihara





### HU HUMANITIES PROFESSOR GETS JICA PRESIDENT AWARD

A professor from Hiroshima University's Graduate School of Humanities and Social Sciences was among the recipients of the 2020 JICA President Award.

Hiroshima University Professor Takuya Baba was among the 48 individuals and organizations chosen by the Japan International Cooperation Agency to get last year's JICA President Award. The annual award commends the preeminent achievements of those working in the field of socio-economic development in developing countries through JICA's international cooperation activities.

Professor Baba's research focuses on mathematics education from the perspective of supporting developing countries and enabling broader international comparative studies. He specializes in lesson study, professional growth of teachers, ethnomathematics, and curriculum development.

For over 20 years, he has contributed to JICA projects in the

field of basic education in Kenya, Zambia, and Bangladesh, among others. Since he was appointed to Hiroshima University's Graduate School of International Cooperation Studies in 2001, he has pioneered programs such as dispatching graduate student volunteers to Zambia, expanding the acceptance of JICA-related international students, and promoting a graduate school collaboration program.

The Zambia Special Education program has helped hone the expertise of junior specialists, consultants, and researchers who would be responsible for future cooperation work.

Professor Baba also spearheaded symposiums on the UN Sustainable Development Goals that links Japan's regional development and international cooperation.

### AMBASSADOR OF BOSNIA AND HERZEGOVINA VISITS HU

On December 17, 2020, H.E. Sinisa Berjan, Ph.D., Ambassador Extraordinary and Plenipotentiary of Bosnia and Herzegovina, paid a courtesy call to the Higashi-Hiroshima Campus of Hiroshima University. The meeting tackled various topics, including the potential for interchange between HU and universities in Bosnia and Herzegovina. It is hoped that this meeting will lead to future exchanges and partnerships with universities and research institutions in Bosnia and Herzegovina.



# PREDICTING DEBRIS FLOW OCCURRENCE TO PREVENT SEDIMENT-RELATED DISASTERS

The Resilience Research Center in Hiroshima University (HRRC) has launched a new project, named "Gagara-Yama Demonstration Experiment of Sediment-related Disasters," aimed at elucidating the mechanism behind slope failures and debris flows to protect lives from sediment-related disasters. The Gagara-Yama mountain, located inside the HU campus, is composed of weathered granite, which is at risk of collapsing during heavy rainfall.

Measurement equipment for groundwater level, water pressure, and temperature have been installed in the area. A satellite positioning, navigation, and timing system will be set up to collect basic data, such as changes in the groundsurface topography.

We welcome research collaborators and appreciate all the support from abroad for our unique activities.

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<u>https://www.hiroshima-u.ac.jp/en/hrrc</u>

# HU's latest PUBLICATIONS

Introducing recently published books and authors from Hiroshima University



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The contents are available in English, so I hope that researchers from around the world will read them. I intend to continue my research and discover unknown Kirishitanban that are lying dormant.

> Associate Professor Jun Shirai



# VOCABULARIO DA LINGOA DE JAPAM

A dictionary that reveals the Japanese medieval language left behind by Jesuit missionaries

Collection of the National Library of Rio de Janeiro Japanese-Portuguese Dictionary

This book is a color reproduction of the Kirishitan-ban Nippo Jisho (Japanese-Portuguese Dictionary) discovered in 2018 by Jun Shirai — associate professor at Hiroshima University's Graduate School of Humanities and Social Sciences — at the National Library of Brazil, in Rio de Janeiro.

The Kirishitan-ban dictionary was published by Jesuit missionaries who visited Japan in the 16th century to propagate the Catholic faith, using the European typographic techniques to understand the Japanese language. It contains 32,000 romanized Japanese headwords annotated in Portuguese.

Since there were no dictionaries with detailed information on the meanings of general vocabulary in medieval Japan, the Japanese-Portuguese Dictionary is a valuable resource for studying the history of the Japanese language - as it includes information on the culture and pronunciation of the Japanese words at the time.

Also, exploring how it came to be in a Brazilian library may help unravel the roots of Brazilian history and culture, including the Portuguese royal family and the Brazilian emperors. Furthermore, the dictionary is valuable as a 400-year-old reference of the Portuguese language.

The one found here is the fourth edition of the Nippo Jisho and the first Kirishitan-ban found in Latin America. The reprint includes a bibliographic introduction and a multifaceted commentary by several authors, including Professor Eliza Tashiro, a research collaborator from the University of Sao Paulo, Brazil.



#### What's in the photo?

HRRC research activities at the area affected by a heavy rain event in July 2018, Hiroshima Prefecture



# TURNING THE ENTIRE SCHOOL INTO A MUSEUM



Naming plaques put up on all 127 species of trees on campus

A project to install naming plaques on trees in the Higashi-Hiroshima campus was launched by student volunteers and university staff from the Hiroshima University Museum and the Higashi-Hiroshima Botanical Garden.

As of 2020, there are 5,545 trees of approximately 127 species planted on the Higashi-Hiroshima campus. In addition to being an important educational resource for Hiroshima University staff and students to learn about nature, seasons, and culture unique to Japan, these diverse trees which bloom and bear fruits with the changing seasons are also popular among the local community.

Among the 5,000 trees, those located along routes that are easily visible to pedestrians and those with great importance and value were chosen. Some 1,000 name plaques will be placed on these selected trees throughout the year. The plaques contain the scientific name, the Japanese name, and a QR code, where smartphone users can access the website of the Digital Natural History Museum of Hiroshima University for detailed and multilingual information about the tree species.

The Higashi-Hiroshima campus is the third largest eco-campus among national universities in Japan, with a total area of approximately 250 hectares. A biota survey started in 2012 confirmed 62 species of endangered plants and animals (as of 2020) living on campus. This number is the highest among the national university campuses in the country.

# HIRAKU 3 MINUTE THESIS COMPETITION 2020



The HIRAKU Three Minute Thesis (3MT) Competition 2020 was successfully held on November 21.

This year's Competition was conducted entirely online, expanding the scope of the eligible participants to all doctorate students enrolled in Japanese universities. There were 62 applications in total, from 24 national, public and private universities. The 20 finalists, who were welcomed to the final stage, were selected as a result of the rigorous screening process of the applicants' videos.

With a substantial gathering of 160 people for the Japanese Division and 335 people for the English Division watching the competition, the finalists managed to showcase their research using only a single slide within a limited time-span of three minutes, in a language appropriate to a non-specialist audience.

At the conclusion of the 3MT Presentations, panel talks with the finalists were presented in both of the divisions, in collaboration with the Japan Science and Technology Agency (JST). The theme of the panel talks was "Our Future Society, Our Future Life," and they were moderated by experienced science communicators Dr. Takayuki Honda (Freelance Science Communicator) for the Japanese Division and Dr. Kazuyoshi Shimada (Director at JST) for the English Division. Under the supporting guidance of the moderators, the finalists enthusiastically discussed and exchanged opinions about how their research could contribute to society in the future.

#### About the Competition

The HIRAKU 3MT Competition aims to develop the doctorate students' presentation and research communication skills while leading to the broader society (as the audience), further enhancing their understanding of doctorate resources and researches.



https://home.hiroshima-u.ac.jp/ hiraku/en/event/competition\_2020/



### NEW BLENDED SOLAR CELLS YIELD HIGH POWER CONVERSION EFFICIENCIES

Researchers at Hiroshima University in Japan have blended together various polymer and molecular semiconductors as photo-absorbers to create a solar cell with increased power efficiencies and electricity generation. These types of solar cells, known as organic photovoltaics (OPV), are devices that generate electricity when light is incident upon their photo-absorbers. The efficiency of a solar cell is determined by comparing how much electricity is generated to how much light is incident upon the cell. This is referred to as "photon harvest", or how many particles of light are converted into electrical current. The more efficient the solar cell, the more cost effective and pragmatic the cell is for commercial use.

The team at the Graduate School of Advanced Science and Engineering added only a small amount of a compound that absorbs long wavelengths of light resulting in an OPV that was 1.5 times more efficient than the version without the compound. The compound was able to enhance the absorption intensity due to the optical interference effect within the device. The group went on to show that how they are distributed is key to further improved power generation efficiency.

"The addition of a very small amount of a sensitizer material to an OPV cell, which consists of a semiconducting polymer that we developed previously and along with other materials," said Itaru Osaka, corresponding author of the paper, published November 2020 in *Macromolecules*. "This leads to a significant increase in the photocurrent and thereby the power conversion efficiency due to the amplified photon absorption that originates in the optical interference effect. A key is to use a very specific polymer, one that allows us to have a very thick semiconductor layer for OPV cells, which significantly enhances optical interference effect compared to a thin layer."

As for future work, Osaka has his eyes set on pushing the boundaries of state of the art solar cells.

"Our next step is to develop better semiconducting polymers as the host material for this type of OPV and better sensitizer materials that can absorb more photons in the longer wavelength regions. This would lead to the realization of the world's highest efficiency in OPV cells."

#### About the study

Saito, M., Tamai, Y., Ichikawa, H., Yoshida, H., Yokoyama, D., Ohkita, H., & Osaka, I. (2020). Significantly Sensitized Ternary Blend Polymer Solar Cells with a Very Small Content of the Narrow-Band Gap Third Component That Utilizes Optical Interference. *Macromolecules*, 53(23), 10623–10635.

https://doi.org/10.1021/acs.macromol.0c01787

# MEDICAL ODDITY USHERS IN DISCOVERY OF UNHEARD-OF 'IMMUNITY GENE' MUTATIONS

#### Researchers baffled by an infant's rare encephalitis case unusual in children found unheard-of mutations and a new way to examine the "immunity gene."

An infant's odd case of rare encephalitis not typically found in children led researchers to discover never before seen genetic mutations and a more accurate technique to examine the IRAK4 gene responsible for innate immunity.

The IRAK4 gene instructs the production of a protein that plays a key role in the early recognition and response to invading pathogens. Inherited mutations in this gene can cause an immune system disorder that leaves the body susceptible to recurrent infections of pus-forming pyogenic bacteria. Cases of IRAK4 deficiency are quite rare and only about 10 familial instances were identified so far in Japan.

A Hiroshima University-led research team detected two novel IRAK4 mutations, c.29\_30delAT (p.Y10Cfs\*9) and c.35G>C (p.R12P), in a 10-month-old boy with anti-Nmethyl-d-aspartate receptor (anti-NMDAR) encephalitis and human herpesvirus 6 (HHV6) reactivation. The p.Y10Cfs\*9 and p.R12P variations were inherited from his father and mother, respectively. The research team found the mutations by using whole exome sequencing (WES), a method used to exhaustively examine the DNA for genetic disorders.

Anti-NMDAR encephalitis, an inflammation of the brain, happens when the immune system attacks a vital brain receptor, causing psychiatric symptoms, involuntary movement, seizures, autonomic dysfunction, and central hypoventilation. It typically occurs in adult females suffering from ovarian tumor. Only a few cases of anti-NMDAR encephalitis have been so far reported in infants.

The researchers suspect that reactivation of HHV6 may have induced brain damage that triggered the production of anti-NMDAR antibodies.

"It is well known that anti-NMDAR encephalitis is triggered by HSV1 (herpes simplex virus) infection. The post -infectious autoimmune process that follows the HSVinduced brain damage is thought to be the cause of anti-NMDAR encephalitis," the researchers said in their study published in the Journal of Clinical Immunology.

"The coexistence of anti-NMDAR encephalitis and HHV6 reactivation in this patient may reveal an unknown manifestation associated with IRAK4 deficiency," they said.

#### More precise method to analyze IRAK4 mutations

Although the researchers have yet to find direct evidence demonstrating a relationship between IRAK4 deficiency and the development of anti-NMDAR encephalitis or HHV6 reactivation, they were able to establish that mutations p.Y10Cfs\*9 and p.R12P are damaging.



Brain MRI of the 10-month old boy with anti-NMDAR encephalitis obtained on day 4. The axial T2 weighted image (T2WI) in A and B and the axial fluid attenuation inversion recovery (FLAIR) image in C and D showed high intensity regions in the bilateral thalamus. New "immunity gene" mutations that researchers discovered to be deleterious were found in the infant.

The researchers developed a novel NF- $\kappa$ B reporter assay that can precisely evaluate whether an IRAK4 mutation is harmful. The reporter assay allows them to investigate the activation of transcription factor NF- $\kappa$ B which regulates the body's inflammatory responses.

"Using this system, we confirmed that both novel mutations are deleterious. The current case revealed the possibility that genetics can contribute to characterizing infantile cases with anti-NMDAR encephalitis," study author Satoshi Okada, a professor at HU's Graduate School of Biomedical and Health Sciences, said.

They resolved potential issues of misevaluation in a previously developed NF- $\kappa$ B reporter assay by using CRISPR gene-editing technology to remove the IRAK4 naturally expressed in the HEK293 cell – commonly used in studying gene function as it is much easier to transfect than other cell lines.

"HEK293 cells have endogenous IRAK4 expression. Their endogenous IRAK4 prevents the precise evaluation of the activity of introduced WT or mutant IRAK4," Okada explained.

To date, there are so far 24 known mutations identified in patients with IRAK4 deficiency.

The research team hopes to soon introduce their novel NF- $\kappa$ B reporter assay system to help evaluate IRAK4 gene mutations and achieve early diagnosis.

#### About the study

Nishimura, S., Kobayashi, Y., Ohnishi, H. et al. IRAK4 Deficiency Presenting with Anti-NMDAR Encephalitis and HHV6 Reactivation. J Clin Immunol (2020). https://doi.org/10.1007/s10875-020-00885-5

# 'OFF SWITCH' DURING ERROR-PRONE CELL CYCLE PHASE MAY FIX CRISPR'S UNWANTED CHANGES PROBLEM

Turning off gene-editing until it reaches cell cycle phases where more accurate repairs are likely to happen offers a promising fix to CRISPR-Cas9's problem with unwanted genetic changes.

Researchers from Hiroshima University and Tokyo Medical and Dental University published on Communications Biology the results of their study which successfully demonstrated a more precise gene-editing and suppressed unintended genetic deletions, insertions, or mutations called off-target effects.

Although previous methods were developed that reported fewer off-target effects associated with the CRISPR technology, the researchers said these often exhibited lower editing efficiency.

"We aimed to develop the method to avoid the side effect called off-target effect which is one of the most challenging problems in the genome-editing field," said Wataru Nomura, one of the study's authors and a professor at HU's Graduate School of Biomedical and Health Sciences.

"Our method is like hitting two birds with one stone. We can improve the preciseness of genome editing and suppression of off-target effects at the same time."

#### More control in gene-editing

CRISPR-Cas9 has ushered in a new frontier in gene editing as a simpler and less expensive tool. Acting like scissors, it can snip genetic material you want to alter. The process, however, can also create off-target effects that limit its use in the field of therapeutics.

The newest method developed to eliminate off-target effects uses the anti-CRISPR protein AcrIIA4 which works like an "off switch" that stops the genome editing activity of SpyCas9. The researchers fused AcrIIA4 with the N terminal region of human Cdt1 – a gene that helps ensure DNA replication happens only once per cell division – intending to deactivate gene editing until S and  $G_2$ , phases of the cell cycle when homology-directed repair (HDR) is dominant.

HDR is one of the two DNA repair processes used by organisms along with non-homologous end joining (NHEJ). Of the two, however, HDR is the preferred method as the repair relies on the existence of two chromosome copies in each cell. HDR's use of the duplicate chromosome as a template for repair makes gene editing more precise as opposed to NHEJ which just tends to connect the broken ends of the DNA. HDR occurs during the S and G<sub>2</sub> phases of the cell cycle while NHEJ operates in all phases, especially in  $G_1$  – the first phase of the cycle's interphase stage where the cell grows in preparation for DNA replication.

The researchers found that the amount of ArIIA4-Cdt1 fusion is dependent on the cell cycle. It increases during the  $G_1$  phase which stops gene-editing from happening and, consequently, halts repairs through NHEJ. Meanwhile, it decreases during the S,  $G_2$ , and M phases that follow.

"The efficiency of HDR using AcrIIA4-Cdt1 was increased approximately by 4.0-fold compared to that using SpyCas9 alone. At target or off-target site 1 (HCN1 gene), the mutation ratio was decreased by 86.5%. Moreover, the mutation ratio at off-target site 2 (MFAP1 gene) was decreased from 8.5% to 0.6% using AcrIIA4-Cdt1," the researchers said in the study.

"Co-expression of SpyCas9 and AcrIIA4-Cdt1 not only increases the frequency of HDR but also suppresses offtarget effects. Thus, the combination of SpyCas9 and AcrI-IA4-Cdt1 is a cell cycle-dependent Cas9 activation system for accurate and efficient genome editing."

Nomura said they want to further improve the preciseness of the system so it could be used safely in the therapeutic field.

"We envision to apply our system to other CRISPR/anti-CRISPR combinations as well as other CRISPR based gene editor such as base editors and targeted transcription mediators," he said.

"Our ultimate goal is to develop a genome editing system which can be used safely in the medical therapeutic field."

#### About the study

Matsumoto, D., Tamamura, H. & Nomura, W. A cell cycledependent CRISPR-Cas9 activation system based on an anti-CRISPR protein shows improved genome editing accuracy. Commun Biol 3, 601 (2020). <u>https://doi.org/10.1038/</u> <u>s42003-020-01340-2</u>

# NEW WAY TO HALT LEUKEMIA RELAPSE SHOWN PROMISING IN MICE

Researchers have identified a second path to defeating chronic myelogenous leukemia, which tends to affect older adults, even in the face of resistance to existing drugs.

Almost all patients with chronic myelogenous leukemia, or CML, have a faulty, cancer-causing gene, or "oncogene" called BCR-ABL1. BCR-ABL1 turns a regular stem cell (a unique type of cell that can turn into other types of cells and then reproduce those cells during life time) in the bone marrow into a CML stem cell that produces malformed blood cells. And instead of the CML stem cell dying when it should be scheduled to do so, the oncogene causes it to keep producing even more of these faulty blood cells.

Advances in treatment since the turn of the millennium have been extremely successful at combatting the disease in patients with this oncogene. Drugs called tyrosine kinase inhibitors (TKI) have completely transformed the prognosis of people with such leukemias, and with fewer of the side effects of other cancer treatments. In most cases, the cancer goes into remission and patients live for many years following diagnosis.

BCR-ABL1 directs the production of an abnormal type of tyrosine kinase, an enzyme that 'turns on' many types of proteins through a cascade of chemical reactions known as signal transduction—in effect communication via chemistry. Miscommunication resulting from the faulty enzyme is what promotes the growth of the leukemic cells. By stopping this communication within CML stem cells, TKI signal transduction therapy inhibits their growth and brings a halt to their production of the malformed blood cells.

However, TKIs only controls the disease; they don't cure it. Drug resistance can develop in a patient because while TKIs work well on proliferative mature CML cells that are actively reproducing, they are less effective at inducing cell death on the part of CML stem cells that are quiescent.

Quiescence is an "idling" stage in the life cycle of a cell in which it basically just rests and hangs out for extended periods of time in anticipation of reactivation, neither replicating nor dying.

"If CML stem cells are in a quiescent phase, they are otherwise left untouched by TKI treatment, and so survive to potentially cause a relapse," said Kazuhito Naka, paper author and an associate professor from Department of Stem Cell Biology, the Research Institute for Radiation Biology and Medicine at Hiroshima University.



CML stem cells, which are the cellular source of the vast majority of CML cells, are reportedly resistant to TKI therapy due to the stem cell quiescence. Thus, the remaining CML stem cells are responsible for the recurrence after TKI therapy.

But the researchers found in mouse models that if they disrupt Gdpd3—a different, non-oncogene gene—then the self-renewal capacity of the CML stem cells is sharply decreased. Gdpd3 directs the production of an enzyme for a particular type of lipid that appears to play a key role in regulating the quiescence of CML stem cells in an oncogene-independent fashion.

In other words, the Gdpd3 gene involved in production of this lipid is largely responsible for the maintenance of CML stem cells. The researchers had broken their quiescence. Crucially, when the researchers disrupted the Gdpd3 gene encoding these lipids, leukemia relapse in the mice was significantly reduced, even when the BCR-ABL1 oncogene was not disrupted.

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This potentially provides another path to arresting these leukemias and maybe other cancers too, beyond having to wrestle with the BCR-ABL1 oncogene.

While the researchers have discovered a new, biologically significant role for this particular lipid in causing the recurrence of CML, they still do not fully understand the precise way this happens. The researchers now want to investigate the mechanisms involved and whether this lipid also plays a role in the quiescence of the cancer stem cells that cause solid tumors, not just in leukemias, and thus in these cancers' recurrence and growth as well. The new findings were published on September 17th in *Nature Communications*.

#### About the study

Naka, K., Ochiai, R., Matsubara, E. *et al.* The lysophospholipase D enzyme Gdpd3 is required to maintain chronic myelogenous leukaemia stem cells. *Nat Commun* 11, 4681 (2020). <u>https://doi.org/10.1038/s41467-020-18491-9</u>

# RESEARCHERS FIND DIRECTION DECIDED BY RATE OF COIN FLIP IN QUANTUM WORLD

Researchers unveil the walking mechanism of quantum walks, introducing a way to potentially control the direction of movement.



Flip a coin. Heads? Take a step to the left. Tails? Take a step to the right. In the quantum world? Go in both directions at once, like a wave spreading out. Called the walker analogy, this random process can be applied in both classical and quantum algorithms used in state-of-the -art technologies such as artificial intelligence and data search processes. However, the randomness also makes the walk difficult to control, making it more difficult to precisely design systems.

A research team based in Japan may be moving toward a more controlled walk by unveiling the mechanism underlying the directional decision of each quantum step and introducing a way to potentially control the direction of movement. They published their results on October 16 in Scientific Reports, a Nature Research journal.

"In our study, we focused on the coin determining the behavior of the quantum walk to explore controllability," said paper author Haruna Katayama, graduate student in the Graduate School of Integrated Arts and Sciences at Hiroshima University.

In classical systems, the coin directs the walker in space: right or left. In quantum systems, a coin is infinitely less reliable, since the walker operates both as a particle stood in one space and as a wave stretched out in every possibility across time.

"We introduced the time-dependent coin of which the probability of landing on heads or tails varies temporally for unveiling the function of the coin," Katayama said.

This time-dependent coin can shift the walker's position, the researchers found, but the wave characteristic of the walker obscured how much physical space the coin controlled.

"We succeeded in clarifying the equivalence of two completely different concepts — the equivalence of the rate of change in coin probability and the velocity of the wave for the first time," Katayama said. "This unveiled mechanism enables us to control the quantum walk on demand by manipulating the coin with preserving the random process, providing core fundamental elements of innovative quantum information processing technologies such as quantum computing."

The researchers determined that how quickly the coin flipped directly affected how quickly the wave moved, resulting in some control of the walker's movement.

"The walking mechanism enables us to tailor quantum walks as we desire by manipulating the coin flipping rate," Katayama said.

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#### In addition, we have found that the quantum walk with the desired trajectory can be realized on demand by designing the coin. Our results open the path towards the control of quantum walks.

This work was supported in part by the Okawa Foundation for Information and Telecommunications.

Other paper authors are Noriyuki Hatakenaka, professor in the Graduate School of Advanced Science and Engineering at Hiroshima University, and Toshiyuki Fujii, professor in the Department of Physics at Asahikawa Medical University.

#### About the study

Katayama, H., Hatakenaka, N. & Fujii, T. Floquetengineered quantum walks. Sci Rep 10, 17544 (2020). https://doi.org/10.1038/s41598-020-74418-w

### SCIENTISTS SHINE NEW LIGHT ON HEAT-DAMAGED HAIR

A new technique allowed researchers to observe in greater detail how heat alters keratin proteins, helping in their search for ingredients that can prevent heat-damaged hair.



A synchrotron radiation-based experimental technique developed at the Hiroshima Synchrotron Radiation Center (HiSOR) helped scientists get useful structural information on keratin proteins during heat treatments.

Researchers have observed in greater detail how heat changes keratin proteins that result in hair damage.

Curling wands and flat irons could fry the keratin proteins that make up about 85% of our hair, turning it dry and brittle over time.

When heated, keratin proteins aggregate and suspend in a solution, much like the hardening of raw eggs when boiled. Circular dichroism spectroscopy used in experiments to observe keratin structure allows light to pass through the solution for measurement. But it can only work when keratin is solubilized and transparent.

Getting an up-close look at the gradual structural changes that heated keratin proteins undergo is a challenge to detect once the proteins are thermally aggregated and suspended in the solution.

But researchers at Milbon Co., Ltd. and Hiroshima University's Hiroshima Synchrotron Radiation Center (HiSOR) developed an experimental technique sensitive enough to allow direct observation of the protein's aggregation process. They used vacuum-ultraviolet synchrotron-radiation — which provided enough illumination to analyze the structure of aggregated keratin proteins — and optimized the positioning of optical elements to prevent the light from scattering.

"This study showed that the synchrotron-radiation-based experimental technique could clearly monitor the alternations of structural components of the keratin protein under the conditions of heat damage, which is difficult by other methods," Associate Professor Koichi Matsuo of HiSOR said. Before this, he explained that they could only see how the proteins look before they were heated and after thermal aggregation – not the process as it happens.

The progressive information on the protein's structural changes will help their search for active ingredients that can suppress heat damage in hair.

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#### Based on this research, we can develop new haircare products capable of curing or suppressing hair damage due to the heat treatment

"By monitoring protein's structural changes, we could rapidly and accurately judge which ingredients can effectively inhibit the structural change of keratin proteins from various candidates of compounds," he explained, adding that they could also get data such as the heatproof temperature for each active ingredient.

The researchers hope their technique could also prove useful in studying other biological phenomena involving protein suspension or aggregation, such as Alzheimer's disease.

"Our technique enables us to analyze the protein structures under various conditions, including physiological ones. The technique would also be useful for elucidating the structural alternation of other suspended or aggregated proteins such as amyloid fibrils and membrane-bound proteins, which is the cause of Alzheimer's disease," he said.

They presented some of their research findings during the 20th annual meeting of the Protein Science Society of Japan held last year.

### AI THAT DETECTS POST-STROKE DEPRESSION TYPE CAN HELP STROKE SURVIVORS GET RIGHT TREATMENT

An AI might soon help stroke survivors get the right treatment by detecting a patient's post-stroke depression type, a frequently seen neuropsychiatric manifestation after a stroke that could impair functional recovery.

An AI developed by Japanese researchers might soon help stroke survivors get the right treatment by detecting a patient's post-stroke depression (PSD) type, a frequently seen but often overlooked neuropsychiatric manifestation after a stroke that could impair functional recovery.

The AI was developed by Hiroshima University (HU) researchers using a probabilistic artificial neural network called log-linearized Gaussian mixture network. The neural network was trained to distinguish between depression, apathy, or anxiety based on 36 evaluation indices obtained from functional, physical, and cognitive tests on 274 patients.

Details about their research that analyzed the relationship between PSD and activities of daily living independence, degree of paralysis, stress awareness, and higher brain function using machine learning are published in Scientific Reports.

#### **Early PSD detection**

The researchers said each PSD type might have different underlying neuroanatomic mechanisms which could have a distinct impact on a patient's functional recovery. And its early detection is crucial to give the appropriate treatment needed by the patient.

"Depression is a highly comorbid neuropsychiatric symptom during the acute and subacute phase after a stroke and has been reported to negatively influence functional and cognitive recovery. Thus, early diagnosis and intervention are crucial for post-stroke depression," study author Seiji Hama, a research associate at HU's Graduate School of Biomedical and Health Science, said.

"However, PSD is multifactorial, and associated neurological symptoms may hinder the detection process. This study is the first step in aiming to accurately diagnose PSD using data obtained in routine practice without any special equipment."

The researchers tested the AI's diagnostic accuracy through the receiver operating characteristic curve which visually evaluates the performance of a machine learning algorithm by giving it an area under the curve (AUC) score. An AUC score of 1.0 means a perfect performance. The PSD detection AI scored above 0.85.

#### Stress threshold hypothesis

Various post-stroke physical disorders, cognitive dysfunction, and mood disorders associated with stress responses are intricately intertwined, making it difficult to understand the cause of PSD and, therefore, making its diagnosis challenging.

It is uncertain whether PSD occurs as part of the mourning process due to the physical impairments after a stroke or if it is brought about by biological factors associated with brain damage.

The study results, however, suggested that reduced stress adaptability due to stroke-induced brain lesions is behind PSD.

"One of the traditional hypotheses on the PSD mechanism was 'threshold hypothesis,' consistent with many previous reports demonstrating the association between the accumulation of lacunar infarcts within the basal ganglia, thalamus, and deep white matter and PSD," they said in their study.

Hama said they intend to conduct detailed analysis using MRI images to further clarify the origins of PSD and improve techniques to diagnose it in hopes of applying the technology to wearable devices. The researchers expect patient rehabilitation would be improved through the early diagnosis and treatment of PSD.

"If this diagnostic technique of PSD becomes possible to test with a wearable device, it will be possible to use it in the local community. By combining it with the test for cognitive function, we would like to verify its application to the preventive effect of strokes," he said.

#### About the study

Hama, S., Yoshimura, K., Yanagawa, A. et al. Relationships between motor and cognitive functions and subsequent post-stroke mood disorders revealed by machine learning analysis. Sci Rep 10, 19571 (2020). https://doi.org/10.1038/s41598-020-76429-z

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With Professor Shoichi Fujimori

# FOR AN HU PROFESSOR, CURVED-SURFACE MATH IS HIS MUSE

Try to think about things of beauty and an equation is probably the last to pop in your head. One look at the zero mean curvature (ZMC) surfaces formula, however, and Professor Shoichi Fujimori was immediately captivated.



Soap films are used in beautiful experiments to physically realize zero mean curvature surfaces.

(Shoichi Fujimori)

"First, we just felt the equation for ZMC surfaces is beautiful and wanted to know the surfaces," Fujimori, who first saw the equation in his junior year as an undergraduate, said. He had since earned his doctorate in mathematics in 2006 and turned his fascination into a career in the field of differential geometry - dealing with the math of curves, surfaces, and manifolds.

Professor Shoichi Fujimori

Engineering

Graduate School of Advanced Science and



A ZMC surface is a surface that takes up the least area with respect to its boundary. And to physically realize the different shapes assumed by ZMC surfaces, beautiful experiments that use soap films are conducted. But what charmed Fujimori the most are the unexpected discoveries in this field. ZMC surfaces have fascinated mathematicians, inspired innovators in designing the future of aerospace engineering, led architects to build superstrong structures using ultra-light materials, and showed how nature chooses its shape.

We chatted with Fujimori to learn more about the topic, the ZMC surface he developed, and the excitement over minimal surfaces' global behavior.

#### About the Q&A

Interview date January 21, 2021

#### Q: Can you tell us about the topic of your research?

**A:** My research topic is differential geometry in mathematics. There is a quantity on surfaces called "mean curvature." In Euclidean space, a zero mean curvature (ZMC) surface is a surface at which each point of the surface has a neighborhood that is the surface of least area with respect to its boundary. Such soap films — not soap bubbles trapping air — are physical models of ZMC surfaces. ZMC surface theory is one of the classical subjects in differential geometry. In my research, we have developed a fundamental framework of ZMC surfaces in space-time, not in space. I have been studying this topic for about 10 years. The number of researchers who work on this topic is gradually increasing in Europe and Asia.

# Q: Can you share more about the ZMC surfaces framework you developed?

**A:** There was a local construction method for ZMC surfaces in space-time. But there is no guarantee that the surface can be extended globally. In other words, applying the above method, we can locally construct a ZMC surface, but

when we extend the surface, the surface may have singularities. The singularity of a surface is a point where the surface is not smooth, something like a cusp. We then gave some conditions so that the surface can be extended globally, and constructed a lot of ZMC surfaces without singularities.

#### Q: What's the next step in your research?

**A:** My dream is to find all of ZMC surfaces in space-time. But this is really my ultimate goal and I know we cannot solve this issue by ourselves. So I hope many people become interested in our research project and develop our work.

#### Q: Do you have a favorite ZMC surface?

**A:** My favorite ZMC surface in space-time is Schwarz Dtype ZMC surfaces because these surfaces are the first example of ZMC surfaces in space-time with non-trivial topology. It is hard to explain what "topology" is, but intuitively "non-trivial topology" means "complicated shape."

Editor's Note: The full interview is available on the <u>Hiroshima University website</u>.



# SCHOOLS AND GRADUATE SCHOOLS

# SCHOOLS (UNDERGRADUATE)

For undergraduate level, Hiroshima University consists of 12 schools which provide undergraduate courses including majors in the natural sciences, humanities, the social sciences, and many others.

School of Integrated Arts and Sciences School of Letters School of Education School of Education School of Economics School of Science School of Medicine School of Medicine School of Dentistry School of Pharmaceutical Sciences School of Engineering School of Applied Biological Science School of Informatics and Data Science

# GRADUATE SCHOOLS

Graduate level studies at Hiroshima University consist of 4 graduate schools below.

Graduate School of Integrated Sciences for Life Graduate School of Biomedical and Health Sciences Graduate School of Humanities and Social Sciences Graduate School of Advanced Science and Engineering

# ADVANCED COURSE

Special Course of Special Needs Education

### INTERDISCIPLINARY GRADUATE EDUCATIONAL PROGRAM

In addition, three unique program offerings combine graduate level academic coursework with integrative research components.

Phoenix Leader Education Program (Hiroshima Initiative) for Renaissance from Radiation Disaster

TAOYAKA PROGRAM for creating a flexible, enduring, peaceful society

The Frontier Development Program for Genome Editing





### **NEW SPACES ON CAMPUS**

HU libraries in the Higashi-Hiroshima and Kasumi campus reopen after renovation!







#### Voices from Graduates



"Japan — and specially Saijo — has a great environment for studying since it's quiet and people are very friendly. Here at HU, we learned about new research methods that we'll apply once we go back to Indonesia," said Astriyany and Suhaila Marisa, both master's degree graduates from the Graduate School of International Development and Cooperation.



# FIND MORE ABOUT HU

### HU OFFICIAL WEBSITE – ENG

Latest News, Events and Research, as well as links to each university section are available from this webpage.



https://www.hiroshima-u.ac.jp/en



### **HU PROMOTIONAL VIDEO**

Wondering what it's like at Hiroshima University? Here's our new video introducing our campuses and the mesmerizing sights of Hiroshima Prefecture.





https://youtu.be/r1Wg7oQZHYs



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HIROSHIMA UNIVERSITY UPDATE

### UPDATES FROM OUR LABORATORY

This webpage is the source for visitors worldwide to stay updated about what happens in the lab at HU.



https://www.hiroshima-u.ac.jp/en/ laboratory-updates



### **EXPERIENCE HU**

Seasonal video series in collaboration with HU students

Experience HU started in January 2020, intending to transmit the beauty of our campuses from the students' perspective. A group of four students participated in the project by working on the planning, shooting, and editing of the videos with the guidance of PR staff. They were Akito Nakano and Yuta Hirose from the Graduate School of Advanced Science and Engineering, Daisei Sakai from the School of Economics, and Hiroyuki Hirose from the School of Engineering.

Due to the spread of COVID-19, part of the videos used in the footage was from the previous years. Regardless, the final videos wonderfully conveyed our campus atmosphere. We hope this project gives the general public a sneak-peek into HU's campus life.

Check out the winter edition here







HU LinkedIn

UNIVERSITY OF WORLD-WIDE REPUTE AND SPLENDOR FOR YEARS INTO THE FUTURE





Morning at Hiroshima University Satake Memorial Hall, Higashi-Hiroshima Campus