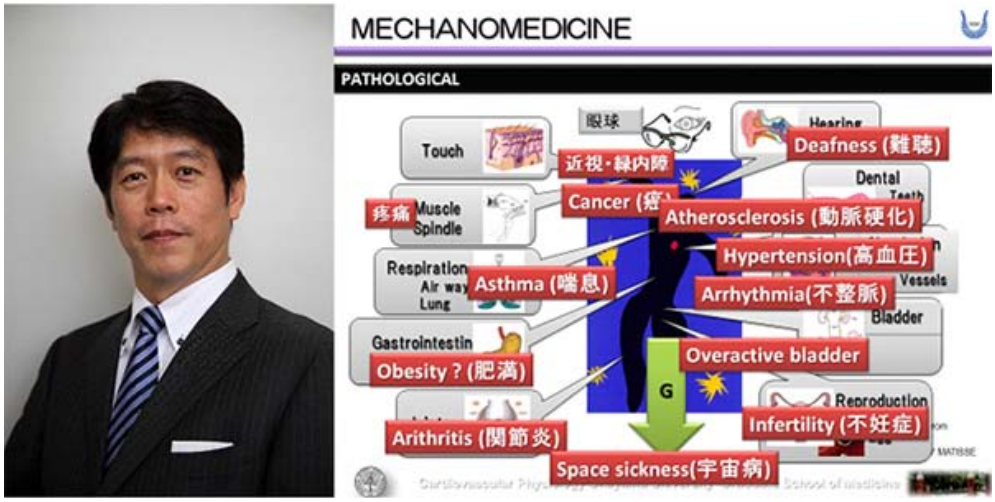
OKAYAMA UNIVERSITY e-Bulletin



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News

Professors Jian Feng Ma and Naoki Yamaji receive "Highly Cited Researchers 2015" Award

A ceremony was held at Okayama University on April 27 to present Professor Jian Feng Ma and Associate Professor Yamaji Naoki—who are both affiliated with the Institute of Plant Science and Resources (IPSR)—with the Highly Cited Researchers 2015 award, which is awarded annually by Thomson Reuters to researchers in wide ranging fields of science whose work has attracted particularly high attention.

Professor Ma (left) and Associate Professor Yamaji receive their awards during the ceremony

Recipients of the Highly Cited Researchers award are selected by analyzing citations and related statistics in scientific literature in related fields to determine research that has had strong impact for a given year. This year's award was given to 3,126 scientists around the world, including 80 from Japan. This was the first time that individuals from Okayama University received the honor—and the fact that two professors were selected is nothing short of groundbreaking.

From left: President Morita, Professor Ma, Associate Professor Yamaji and Executive Director Yamamoto

Account manager Sayaka Miwa participated in the ceremony as a representative from Thomson Reuters, while the participants from Okayama University were President Kiyoshi Morita, Executive Director and Vice President for Research Shinichi Yamamoto, and representatives from University Research Administrators (URAs). "The fact that two talented researchers from our institution were selected for the Highly Cited Researchers award makes me extremely proud, and I am looking forward to the continuing work of both Professor Ma and Associate Professor Yamaji," commented President Morita by way of encouragement.

Both professors have worked on identification of mineral transporters and clarifying plants' resistance mechanisms toward mineral stress, which is a type of plant stressor that includes nutritional deficiency and excess toxic mineral elements. Their research into the mechanisms that plants use to acquire the nutrients necessary for growth and direct them towards their organs—as well as both scholars' comprehensive clarification of the mechanism through which plants divest poisonous metals of their toxicity, all the way from the level of the field to that of the gene—have been nothing short of dynamic. The selection of the professors for this award reflects how their research contributions are on the global cutting edge.

News

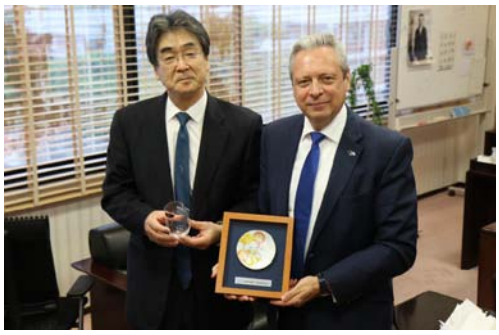
Ambassador of the European Union Delegation to Japan gives a lecture on "European Higher Education in the World"

On June 29, 2016, the ambassador of the European Union Delegation to Japan, His Excellency Viorel Isticioaia-Budura delivered a lecture at Okayama University.

Prior to the lecture, the ambassador visited the President of Okayama University, Dr Kiyoshi Morita, who gave an overview of education and research at the University. There was also an opportunity for a group of staff, faculty, and students to exchange opinions with the Ambassador. Later, there was a meeting on campus at the L-cafe with approximately 50 local and international students, and other interested parties. It was a rare and valuable opportunity to hear the ambassador's comments and observations about the EU and current events such as Brexit, and the attendees listened intently to the active exchanges.

His Excellency then gave his lecture entitled "European Higher Education in the World: Strengthening the Ties That Bind Us" at the 50th Anniversary Hall on the Tsushima campus to an audience of 250 people from throughout the university. The ambassador introduced the origins and the economic and social achievements of the European Union, before moving on to the friendly relations with Japan as a strategic partner, relating success stories of academic cooperation, and the important role that the Japanese have played in higher education in the EU.

University President Morita (front row, third from the right) as Ambassador Isticioaia-Budura (front row, fourth from the right) pays his courtesy call.



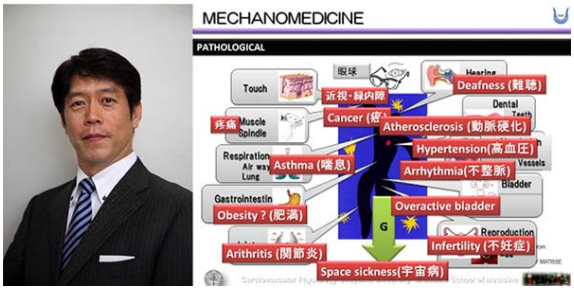
Exchange of memorial gifts.

Ambassador Isticioaia-Budura answering a student's question during the exchange meeting at the L-cafe.

The 50th Anniversary Hall during Ambassador Isticioaia-Budura's address.

Feature

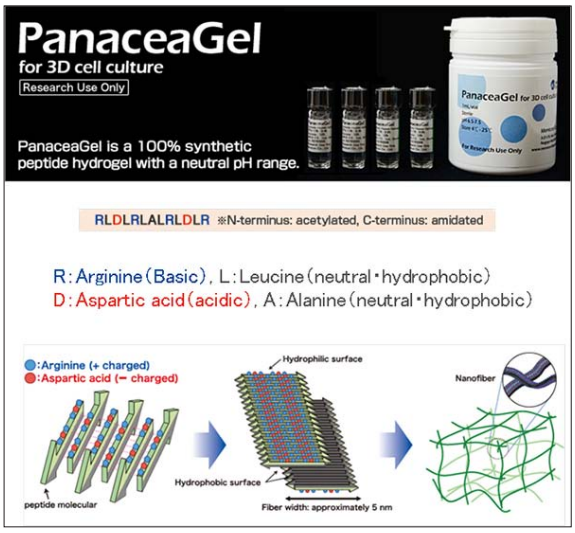
MECHANOMEDICINE: Insights into mechanical stress in clinical medicine



CSO& CEO, STREX INTERNATIONAL, LLC
ADVISOR, MENICON

Keiji Naruse is renowned for this research on 'mechanobiology'—a term that he created to describe and visualize his work that integrates the mechanics of human tissue. "My interest in the mechanical aspects of the body began as a medical student," says Naruse. "I recall asking a lecturer about why cells and tissues expand and contract and being told to 'find out for yourself'. So that was the beginning of my research on 'mechanobiology'."

The sense of touch registered by our skin, sudden increases in the heartrate during exercise, and the vibration of the liquid inside the cochlea are examples of the effects of stimuli on our body. In their research, Naruse and colleagues are addressing issues including how mechanical stress (stretching and shear) affects the cardiovascular system (myocardial regeneration/arrhythmia), reproductive system (sperm separation and fertilized egg culture) and medical materials (hemostatic agents).



PanaceaGel

Importance of translational research and establishing bio-venture companies

"I firmly believe in commercializing ideas and research findings," says Naruse. "I am working with partners both in Japan and overseas on translating our research into healthcare products."

To address infertility, Naruse and his colleagues have focused on the importance of mechanical stress in the oviduct for fertilization—mechano-reproduction—and developed the 'Improved Human Assisted Reproductive Technology' (iHART). This protocol consists of a Microfulidic Sperm Sorter (Qualis) and Tilting Embryo Culture System (TECS). "Our mechano-reproduction research is based on integrating microfluidics with materials used for producing soft contact lens," explains Naruse. "This system was approved by the FDA in June 2014. It is in use at clinics in Japan."

Qualis Sperm Sorter (In Japanese)
http://menicon-lifescience.com/qualis.html

Another example of an idea taken from the lab to patient care is the 'panaceaGel'— a neutral self-assembling peptide hydrogel— used as a scaffold in three-dimensional cell culture and as a carrier for drug delivery. Another important application of this material is as a coagulant to rapidly stop bleeding: The Neutral Self-Assembling Peptide Hydrogel SPG-178 as a Topical Hemostatic Agent, PLOS One, July 21, 2014, http://dx.doi.org/10.1371/journal.pone.0102778.

PanaceaGel
http://menicon-lifescience.com/english/panaceagel.html

Information about STREX Inc
http://www.menicon-lifescience.com/english/

Mechanical Cell Stretch System

Future

"I am continuing to expand our research on mechanobiology and applications of mechanical stress-inducing instruments for the life sciences," says Naruse. "Projects on the horizon include space medicine in collaboration with Japanese astronauts working in the International Space Station. There are still many unexplored frontiers in cell response to mechanical stimuli."

Sperm Sorter

Selection of publications

- Stretch and microfluidics
  "Laminar flows: Subcellular positioning of small molecules"
  Nature 411, 1016 (28 June 2001)
  doi:10.1038/35082637
  http://www.nature.com/nature/journal/v411/n6841/full/4111016a0.html

- Calcium influx through stretch activated channels
  "Ca2+ influx and ATP release mediated by mechanical stretch in human lung fibroblasts"
  Biochemical and Biophysical Research Communications , vol.453, 101 - 105, October 2014.

doi: 10.1016/j.bbrc.2014.09.063
http://www.sciencedirect.com/science/article/pii/S0006291X1401688X

- Generation of temporally controlled cardiac-specific TRPV2-deficient mice
"TRPV2 is critical for the maintenance of cardiac structure and function in mice"
Nature Communications 5, Article number: 3932 (2014)
doi:10.1038/ncomms4932
http://www.nature.com/articles/ncomms4932

- Mechano-cardiovascular: Stretch-induced arrhythmia
"Effect of azelnidipine and amlodipine on single cell mechanics in mouse cardiomyocytes"
European Journal of Pharmacology, vo. 715, 142-146, September 2013.
doi: 10.1016/j.ejphar.2013.05.030
http://www.sciencedirect.com/science/article/pii/S0014299913004378

- Stretching of single cardiomyocyte
"Load dependency in force–length relations in isolated single cardiomyocytes"
Progress in Biophysics and Molecular Biology, vol.115, 103-114, August 2014.
doi: 10.1016/j.pbiomolbio.2014.06.005
http://www.sciencedirect.com/science/article/pii/S0079610714000479

Further information

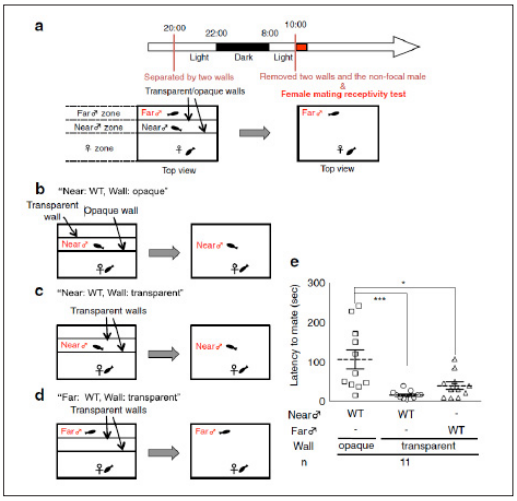
Keiji Naruse, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences
http://soran.cc.okayama-u.ac.jp/view?l=en&u=ffa8175b01c957f574506e4da22f6611

Research Highlights

Mate-guarding behaviour favours a familiar face

Okayama University researchers confirm the role of mate-guarding in males for blocking the female's visual familiarity with rival males to improve mating success in a medaka fish model.

"Male-male competition and female mate choice are considered to be major constituents of mating strategies and many studies of these behaviors have been performed individually," explain Hideaki Takeuchi at Okayama University and the University of Tokyo and his collaborators in Japan and the US in their report. Previously, this team reported that male medaka fish in a triangle relationship (two males and one female) hold a position between the rival male and a female, which results in improvement of mating success. However the significance of different effects from this mate-guarding behaviour –such as visual familiarity and apparent social dominance – had not previously been understood.



Novel visual familiarization system with separation condition (a) Time-course of the female mating receptivity test. A case of far focal male is shown. (b-d) Separation conditions for the female mating receptivity test in dyadic relationships. Fish were randomly picked from two communal tanks each containing four males and four females and the same males were used several times in the three conditions. (b) "Near: WT, Wall: opaque" The female couldn't see the male in the near zone and mated with it the next morning. (c) "Near: WT, Wall: transparent" The female could see the male in the near zone from a close proximity and mated with it the next morning. (d) "Far: WT, Wall: transparent" The female could see the male in the far zone from some distance and mated with it the next morning. (e) Visual familiarization enhanced female receptivity even if the male was located in the far zone. Mean ± SEM. ***P ← 0.0001

The researchers used a transparent aquarium split into 3 compartments with the female in the end compartment. Male and female fish were selected at random and stored in the compartments for around 12 hours overnight before being released to mate.

The enhanced female receptivity (the decreased latency to mate) with transparent walls versus opaque walls confirmed the importance of visual familiarity. The team also quantified the mate guarding behaviour of the near fish and confirmed that by blocking the far fish from view, they impeded the visual familiarization in the far fish. Mutant fish that have mate-guarding behaviour deficits did not inhibit the mating success of the far fish.

The importance of visual familiarity was further corroborated in tests distinguishing the dominant males from their preceding mate-guarding behaviour. When a separation procedure was then used to block the dominant males from view, the dominant males fared unfavourably in offspring paternity tests.

Mating criteria for different species range from plumage and colouring to behavioural dominance and visual familiarity. The researchers suggest that female mate preference for familiar mates may help ascertain social dominance in males.

Publication and Affiliation

Saori Yokoi[1,2], Satoshi Ansai[3], Masato Kinoshita[3], Kiyoshi Naruse[2], Yasuhiro Kamei[2], Larry J. Young[4], Teruhiro Okuyama[1,5] and Hideaki Takeuchi[1,6*]Mate-guarding behavior enhances male reproductive success via familiarization with mating partners in medaka fish.
2016 Frontiers in Zoology 13 21

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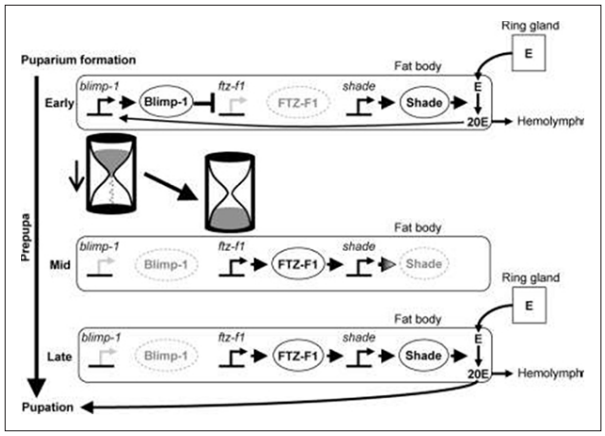
Research Highlights

Molecular "sands of time" identified for fruitfly development

Okayama University have identified genes and processes responsible for pupation timing in the development of fruit fly larvae into adult insects.

The timing mechanism between specific developmental stages such as pupation in insects is so far little understood. In the *Drosophila melanogaster* – or common fruit fly - it is known that a pulse of the molting hormone ecdysone (E) is released to initiate the transition of the larva into a "prepupa" and a second pulse 10 hours later is then thought to induce pupation at around 12 hours. Using knock down models and forced expression of normal or modified proteins Hiroshi Ueda and colleagues at Okayama University investigated the role of different proteins on the timing of this 12 hour interval.



An hourglass model for molecular mechanism to determine pupation timing. At the early prepupal stage, the *ftz-f1* gene is repressed by Blimp-1 during high levels of 20E. The *shade* gene is expressed independent of βFTZ-F1 and disappears by mid-prepupal stage. After the decline of 20E levels, Blimp-1 and its mRNA degrade rapidly (Agawa et al., 2007; Akagi and Ueda, 2011) allowing expression of βFTZ-F1 which induces Shade in the fat body at late prepupal period. Then Shade converts released E to 20E, inducing pupation.

Shade, a protein mainly expressed in an insect organ that stores fat and is also known to sense nutrition – "fat body" - converts the hormone E into its active form 20-hydroxyecdysone (20E). Ueda and colleagues found that knock down of the *shade* gene in fat body delayed pupation whereas knockdown of the *shade* gene in other organs had no significant effect, confirming a role of fat body in pupation timing. "We think that the fat body may incorporate the nutritional status of the animal and sends a cue for the final decision of pupation,"say Ueda and colleagues in their report.

As for other influencers of pupation timing, the orphan nuclear receptor *β*FTZ-F1 - to which is attached another protein factor Blimp-1 - is known to be expressed after the 20E pulse. The researchers showed that over- and underexpression of *β*FTZ-F1 advanced and delayed pupation respectively. They also confirmed Blimp-1's role as a *β*FTZ-F1 repressor, showing that overexpression of Blimp-1 delayed pupation.

Blimp-1 is soon degraded – a protein conserved in mammals too. Studies with a line of Blimp-1 modified to enhance its stability led to delayed pupation and of the reduction of Blimp-1 expression led to advanced pupation. The researchers describe the naturally occurring Blimp-1 as like "sands in an hourglass". As the Blimp-1 molecules degrade and levels fall, *β*FTZ-F1 levels increase to initiate pupation. They also showed the advantage of repressor molecule such as Blimp-1 to use precise time measuring.

Publication and Affiliation

Kazutaka Akagi[1, 3*], Moustafa Sarhan[1, 4*], Abdel-Rahman Sultan[1, 4*], Haruka Nishida[1*], Azusa Koie[1], Takumi Nakayama[1] and Hitoshi Ueda[1,2‡] A biological timer in the fat body comprised of Blimp-1, βFTZ-F1 and Shade regulates pupation timing in Drosophila melanogaster.2016 *Development* doi: 10.1242/dev.133595

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Research Highlights

Barley dormancy mutation suggests beer motivated early farmers

Okayama University have identified the gene mutation and the enzyme it encodes to determine whether the dormancy of barley is long (better for food crops) or short (better for beer-making).

Effects of *qsd1* (left) and *Qsd1* (right) alleles on seed germination after five weeks of 25° C dormancy reduction treatment.

The authors of this paper note that, "The wild barley's long dormancy means that, initially, the grain will not germinate in response to transient moisture availability and will therefore survive hot, dry summers". As a result seeds like wild-type barley that undergo a long state of "dormancy" at maturity – during which they will not germinate –are favoured for food crops. In contrast a short dormancy is more efficient and preferable for beer making.

Kazuhiro Sato and colleagues – a collaboration of Okayama University and the Institute of Agrobiological Sciences in Japan and the University of Adelaide in Australia - compared DNA sequences of Haruna Nijo – a type of barley known to have short dormancy – with wild barley H602, known to have long dormancy. After studying over 5000 plants, they identified the section of the barley's DNA that varies with expression of long or short dormancy - *AK372829*.

The gene *AK372829* codes the enzyme alanine aminotransferase (AlaAT), which is known to play a pivotal role in nitrogen and carbon pathways and protein synthesis, and has been implicated in stress responses to low oxygen and nitrogen availability. Further experiments investigated variations in the nucleotide – that is, single nucleotide polymorphisms (SNPs) – as well as the structure and diversity of the protein associated with short dormancy.

Haruna Nijo has a dominant short dormancy allele *Qsd1*, whereas H602 has a recessive long dormancy allele *qsd1*. The results indicate that Haruna Nijo shares ancestry from long dormancy food-producing barley, suggesting "specific selection of reduced dormancy for the malting process". As the researchers conclude in their report of the work, the selection and exploitation of the plants expressing the *Qsd1* mutation for short dormancy "contributes further to the debate as to what extent the development of ancient agrarian societies was driven by the human appetite for flour and bread, or for beer and alcohol."

Publication and Affiliation

Kazuhiro Sato[1], Miki Yamane[1], Nami Yamaji[1], Hiroyuki Kanamori[2], Akemi Tagiri[2], Julian G. Schwerdt[3],Geoffrey B. Fincher[3], Takashi Matsumoto[2], Kazuyoshi Takeda[1] & Takao Komatsuda[2] Alanine aminotransferase controls seed dormancy in barley. *Nature Communications* 87, 11625 (2016).

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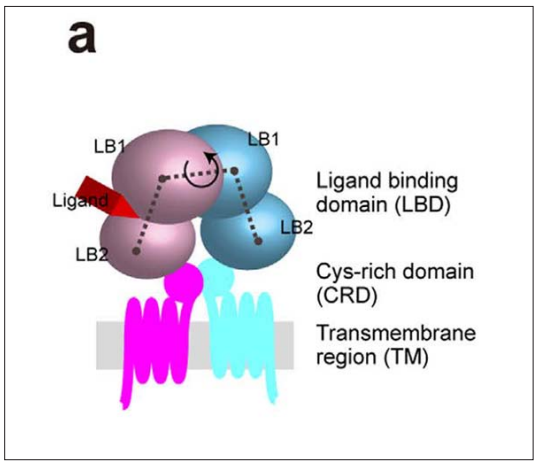
Research Highlights

Fishy approach reveals how things taste sweet or umami

Okayama University have identified the protein conformational changes associated with sweet and umami taste recognition.



Yamashita and colleagues identified the structure and conformational changes in type 1 taste receptor proteins during the recognition of sweet and umami tastes

Taste recognition occurs as specific protein receptors in the mouth interact with molecules in eaten food. The proteins responsible for tasting sweet and umami molecules are described as taste receptor type 1 (T1r) and are common to vertebrates in general, including fish, birds and mammals. It is known that the T1r family of variants interact with food molecules in paired up structures - "heterodimers" – to allow the distinction between umami, sweet, and other tastes. However, difficulties in producing and purifying these proteins have inhibited attempts to directly investigate what interactions occur during sweet and umami taste recognition.

Atsuko Yamashita and a team of researchers at RIKEN SPring-8 Center, the National Institute of Natural Science, the Graduate University for Advanced Studies (SOKENDAI), the Food Research Institute, Osaka University, Okazaki Institute for Integrative Biosciences, and Okayama University have now successfully demonstrated a way around these difficulties. They identified a fish known as medaka or "Japanese rice fish" as a suitable vertebrate model for investigating umami and sweet tastes.

The researchers found they could produce – "express" – the ligand binding domain of the T1r2 and T1r3 proteins in medaka fish as functional heterodimeric proteins. They express the proteins in a glycosylated form, which is closer to the physiological state.

The study identifies the conformational changes the proteins undergo during sweet and umami taste recognition for the first time. The results suggest that venus-flytrap structures in the protein dimers are keys to their ability to transmit the sweet and umami information to our bodies through conformational changes.

Publication and Affiliation

Eriko Nango[1], Shuji Akiyama[2,3], Saori Maki-Yonekura[1], Yuji Ashikawa[1,†], Yuko Kusakabe[4], Elena Krayukhina[5], Takahiro Maruno[5], Susumu Uchiyama[5,6], Nipawan Nuemket[1,7,‡],

Koji Yonekura[1], Madoka Shimizu[4], Nanako Atsumi[7], Norihisa Yasui[7], Takaaki Hikima[1], Masaki Yamamoto[1], Yuji Kobayashi[5] & Atsuko Yamashita[1,7] Taste substance binding elicits conformational change of taste receptor T1r heterodimer extracellular domains. *Scientific Reports*, 6, 25745 (2016).

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Topics : Okayama Travelogue

Setouchi Triennale 2016

The Setouchi Triennale 2016 is held over three sessions (spring, summer and autumn) and runs for 108 days in total. This year's last chance to go island hopping at this site specific contemporary arts festival is from October 8th to November 6th. Spread over 12 islands in the Seto Inland Sea as well as the ports of Takamatsu and Uno, the festival aims to revitalize the islands in the Seto Inland Sea.

The spring, summer, and autumn sessions include about 200 art sites to visit. Autumn events include an outdoor performance of Shogo Ota's last play by theater troupe "Torikouen" in a rice field Karato; contemporary art exhibitions, including the Red Pumpkin on Naoshima island; titanium sculpture (Sea's Memory) in the Uno Port area; and exhibitions by resident artists at the Awashima Artist's Village. Detailed information about access, tickets, and events is posted on the websites listed below.

Further information

Setouchi Triennale 2016
http://setouchi-artfest.jp/en/about/place.html

Artworks
http://setouchi-artfest.jp/en/artworks-artists/artworks/naoshima/

Artists
http://setouchi-artfest.jp/en/artworks-artists/artists/

Setouchi Triennale 2016


"Red Pumpkin" ©Yayoi Kusama, 2006 Naoshima Miyanoura Port Square
Photo: Daisuke Aochi


The Sea's Memory, Haruyuki Uchida


Awashima Artist's Village/HIBINO SHOGAKKO Awashima Lab.

