

Floor map and contact information for organizations related to Tottori Bio Frontier
(Tottori University Yonago Campus)

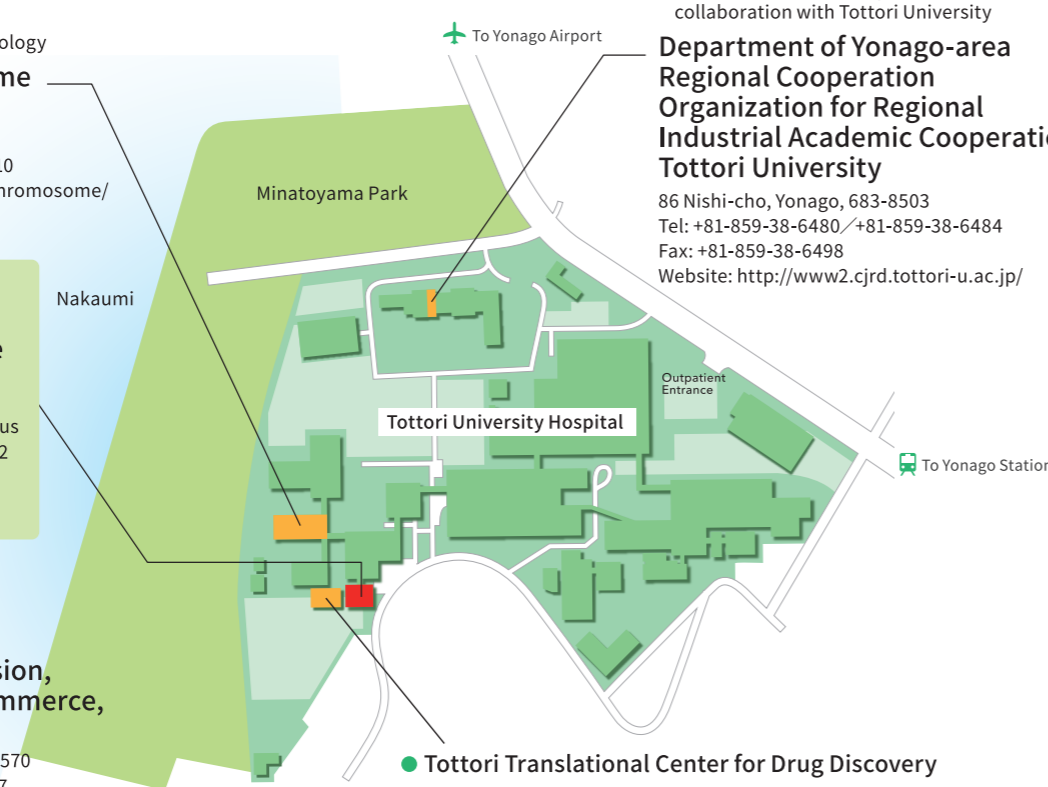
● Inquiries about Tottori University's chromosome medical engineering technology
Tottori University Chromosome Engineering Research Center
 86 Nishi-cho, Yonago, Tottori 683-8503
 Tel: +81-859-38-6212 / Fax: +81-859-38-6210
 Website: <http://www.med.tottori-u.ac.jp/chromosome/>

● Tottori Bio Frontier Management and Administration
Bio Frontier Promotion Office
 Tottori Industrial Promotion Organization
 86 Nishi-cho, Yonago, Tottori 683-8503
 Within the Tottori University Yonago Campus
 Tel: +81-859-37-5131 / Fax: +81-859-37-5132
 E-mail: tbf@toriton.or.jp
 Website: <http://www.bio-frontier.jp/>

● Inquiries for Tottori Prefecture
Industrial Advancement Division, Department of Labor and Commerce, Tottori Prefecture
 1-220 Higashi-machi, Tottori, Tottori 680-8570
 Tel: +81-857-26-7244 / Fax: +81-857-26-8117
 Website: <http://www.pref.tottori.lg.jp/shoukou/>

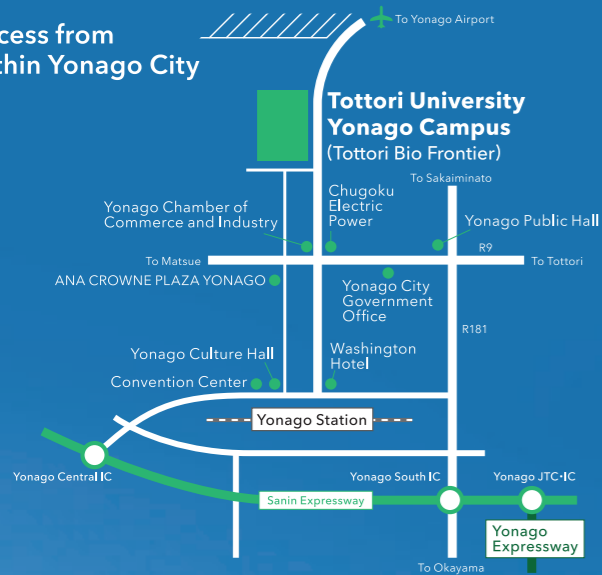
● Inquiries about industry-academia collaboration with Tottori University
Department of Yonago-area Regional Cooperation Organization for Regional Industrial Academic Cooperation Tottori University
 86 Nishi-cho, Yonago, 683-8503
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 Website: <http://www2.cjrd.tottori-u.ac.jp/>

● Tottori Translational Center for Drug Discovery



Chromosome Engineering Technology for
Medical and Industrial Revolution

Access from within Yonago City



Access from outside Tottori Prefecture

- From Tokyo**
 - 1 h 20 min by air
 - 5 h 30 min by JR Tokaido / Sanyo Shinkansen Line and JR Hakubi Line
- From Osaka**
 - 3 h by JR Sanyo Shinkansen Line and JR Hakubi Line
 - 3 h 20 min by Express Bus

- Access from Yonago Station**
 - Approx. 15 min on foot
 - Approx. 3 min by taxi
 - Approx. 8 min by Yonago City Circulating Bus Service
 - *Approx. 4 min by HINOMARU bus Line from Yonago Station to the University's main gate.

- Access from Yonago Airport**
 - Approx. 20 min by taxi
 - *For airport shuttle bus users, get off at SHIYAKUSHOMAE and walk for about 10 min



Molding the future with chromosome medical engineering

Working as an integrated industry-academia-financial-government unit, we apply industrial concepts to various fields and promote commercialization using world-leading chromosome medical engineering technology as our foundation.

Innovative fundamental chromosome medical engineering technology developed at Tottori University is made widely available to organizations in the healthcare and drug discovery industries. By doing so, we accelerate the non-stop industry creation cycle generated from those sources and help improve people's lives and health.

We have developed the chromosome medical engineering technology for drug discovery and healthcare industries

We have built up world-leading chromosome engineering technology over three decades while investigating cancer suppressing genes and creating complete human antibody-producing mice. We are now attempting to apply this technology to various industrial fields while utilizing the expertise we developed during that process.

We intend to use the benefits of human/mouse artificial chromosomes to achieve results that were not possible with previous gene vectors. Moreover, We feel that we must conduct collaborative research with various pharmaceutical and healthcare-related companies to successfully apply our technologies to drug discovery and genetic and regenerative medicine. We are open to any consultation, from which we can begin with the planning stage.

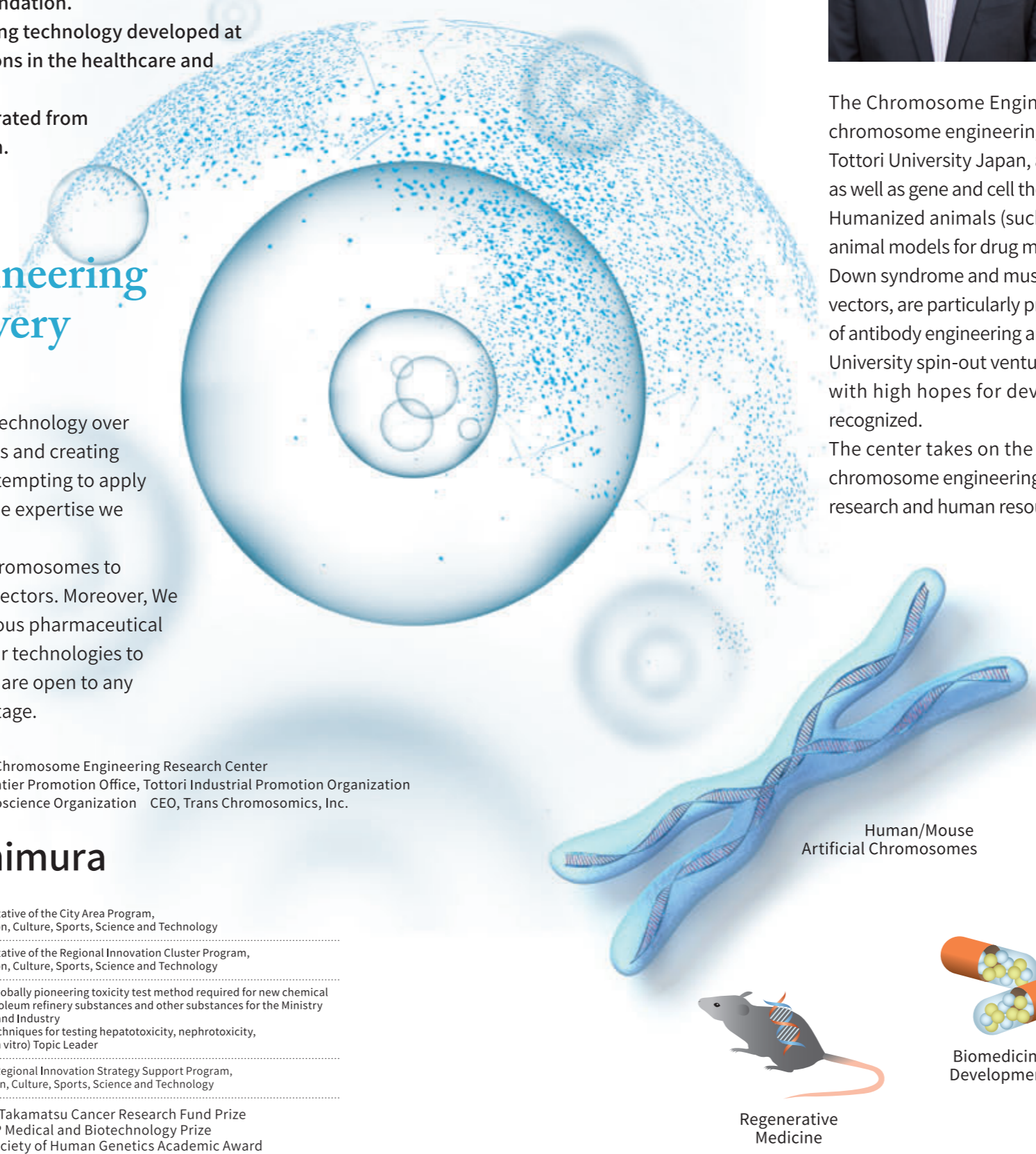


Professor, Tottori University Chromosome Engineering Research Center
 Research Supervisor, Bio Frontier Promotion Office, Tottori Industrial Promotion Organization
 Managing Director, Tottori Bioscience Organization CEO, Trans Chromosomics, Inc.

Mitsuo Oshimura

[PROFILE]

FY 2006 to FY 2008	Research Representative of the City Area Program, Ministry of Education, Culture, Sports, Science and Technology
FY 2010 to FY 2012	Research Representative of the Regional Innovation Cluster Program, Ministry of Education, Culture, Sports, Science and Technology
FY 2011 to the present	Development of a globally pioneering toxicity test method required for new chemical regulations for petroleum refinery substances and other substances for the Ministry of Economy, Trade and Industry (Development of techniques for testing hepatotoxicity, nephrotoxicity, and neurotoxicity in vitro) Topic Leader
FY 2013 to the present	Research Director, Regional Innovation Strategy Support Program, Ministry of Education, Culture, Sports, Science and Technology
Major awards	1993 Princess Takamatsu Cancer Research Fund Prize 1998 Nikkei BP Medical and Biotechnology Prize 2002 Japan Society of Human Genetics Academic Award



Chromosome Medical Engineering: Realizing the Future of Medicine

Institute of Regenerative Medicine and Biofunction, Graduate School of Medical Sciences, Tottori University
 Division of Molecular Genetics and Biofunction, Department of Biomedical Science
 Division of Molecular and Cell Genetics, Department of Molecular and Cellular Biology, School of Life Sciences, Faculty of Medicine (concurrent post)
 Director of the Chromosome Engineering Research Center (concurrent post)

Hiroyuki Kugoh

The Chromosome Engineering Research Center employs the world's most advanced chromosome engineering technology (excising, ligating, and transferring), developed in Tottori University Japan, as a foundation to focus on research that leads to drug discovery as well as gene and cell therapies.

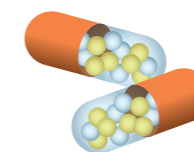
Humanized animals (such as animals producing fully human antibodies and humanized animal models for drug metabolism studies) and model animals of rare diseases (including Down syndrome and muscular dystrophy), developed using human artificial chromosome vectors, are particularly promising because they contribute to evaluation and development of antibody engineering and molecular targeted drugs for next-generation therapeutics. University spin-out ventures, like Trans Chromosomics Inc., Yonago Japan, use the center with high hopes for developing unique, innovative medicine that is internationally recognized.

The center takes on the challenge of "changing the future with chromosomes", using chromosome engineering technology as a solid base and developing globally competitive research and human resources in the academic setting and in society at large.

Human/Mouse Artificial Chromosomes



Drug Discovery Support



Biomedicine Development



Regenerative Medicine

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What are Human/Mouse Artificial Chromosome Vectors?

※1 ※2

We utilized chromosome medical engineering technology developed at Tottori University to create a Human Artificial Chromosome (HAC) from human chromosome 21 and Mouse Artificial Chromosome (MAC) from a mouse chromosome.

These HAC and MAC vectors have special characteristics that are not found in conventional gene transfer vectors.

※1 Kazuki Y, Oshimura M, Mol Ther. 2011 ※2 Takiguchi M et al., ACS Synth Biol. 2012

HAC/MAC Characteristics

▶ Flexible gene insertion

▶ No damage to host chromosomes

Chromosomes are retained and passed on to descendants independently, without integration into the host chromosome

▶ Long term stability for a given copy number

No danger of overexpression or loss of expression

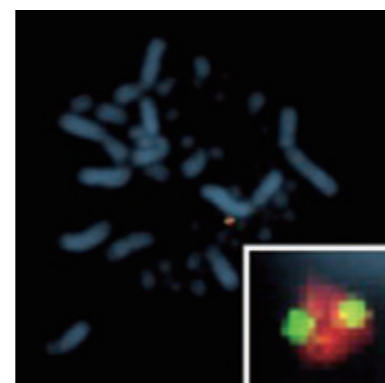
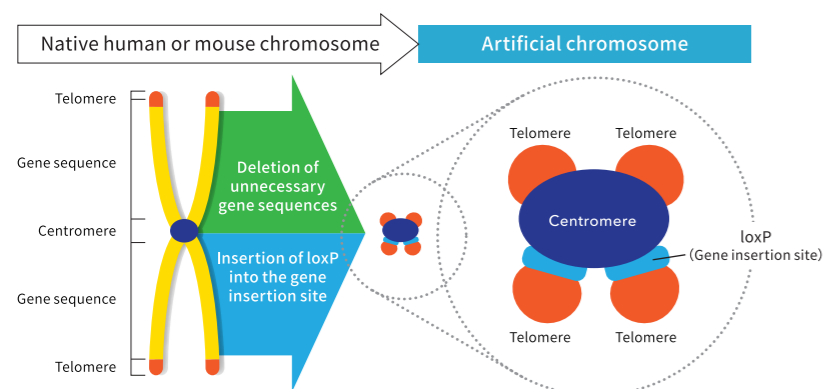
▶ Capable of cell to cell migration

Can be transferred to various types of cells

▶ No limit to the length of DNA they can carry

Capable of simultaneous insertion of huge genes including gene expression control sequences and multiple genes for tissue-specific and stage-specific gene expression.

▶ Breaking down barriers in healthcare and drug discovery with chromosome medical engineering technology.

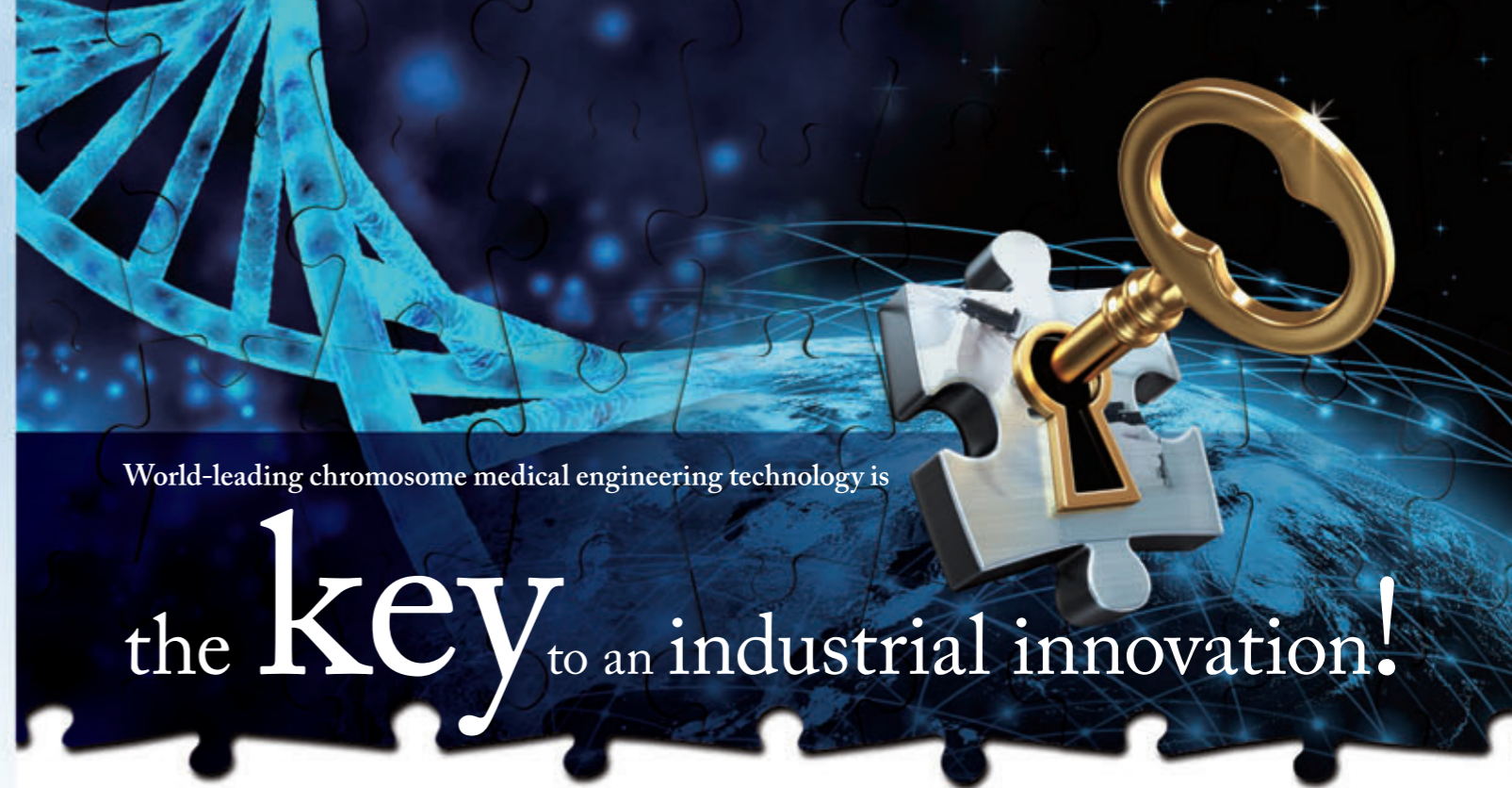


A Human Artificial Chromosome (HAC) vector existing in an animal cell

Awards received

We have received numerous awards in recognition of our chromosome medical engineering technology

- Nikkei BP Medical and Biotechnology Prize (1998)
- Japan Society of Human Genetics Academic Award (2002)
- 10th Congress of the Japanese Society for Regenerative Medicine Young Investigator's Award (2011)
- 39th Annual Meeting of the Japanese Society of Toxicology Investigators' Award (2012)
- 117th OMICS Group Conference, International Conference on Genetic Engineering & Genetically Modified Organisms, Genetic Engineering-2013 OMICS Group Best Poster Award (2013)
- 28th Annual Meeting of Japanese Society for the Study of Xenobiotics, Incentive Award (2013)
- 62nd Annual Meeting of Japanese Association for Laboratory Animal Science, Incentive Award (2015)
- 31st Annual Meeting of Japanese Society for the Study of Xenobiotics, Best Poster Award (2016)
- The Japan Society of Human Genetics, Incentive Award (2016)



World-leading chromosome medical engineering technology is

the key to an industrial innovation!

🔑 Drug Discovery Support Tools

Animal/cell models for human drug metabolism

Species differences exist in drug metabolism and dynamics between humans and experimental animals, and the results obtained from experimental animals do not always apply to humans. We therefore inserted genes involved in human drug metabolism into artificial chromosome vectors and created mice and rats containing these vectors. Those animals have been shown to reproduce drug metabolism in humans, and they may potentially reduce drug discovery costs.

Funding: Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program), Japan Society For The Promotion of Science (FY 2010-2013)

Animal/cell models for human diseases

We use technology that we have developed to transfer chromosomes between cells to create model animals and cells that can reproduce diseases caused by chromosome abnormalities. We are currently pursuing research to reproduce Down Syndrome (trisomy of human chromosome 21) and explain its mechanisms. In the future, we hope to collaborate with drug manufacturers to develop therapeutic agents using these model animals and cells.

Funding: Grant-in-Aid for Scientific Research(S), Japan Society For The Promotion of Science (FY 2013-2017)

🔑 Gene Therapy and Regenerative Medicine

Vector to treat Duchenne muscular dystrophy

Utilizing the benefit that there is no limit to the size of genes that can be inserted, we are attempting to develop a treatment method in which we insert the entire 2.4 Mb of the human dystrophin gene into an artificial chromosome vector and transplant pluripotent cell bearing that chromosome into patients after differentiation into the appropriate cells.

Funding: CREST Basic Research Programs, Fundamental technologies, for medicine concerning the generation and regulation of induced pluripotent stem (iPS) cells, Japan Science and Technology Agency (JST) (FY 2008-2013)

🔑 Safety and Toxicity Assessment System

Animals/cells with reporter genes

The benefits of resistance to silencing of target gene expression and stable retention of genes for a given copy number as well as the ability to insert multiple reporter genes at once can be used to achieve simultaneous assessment and analysis of safety and toxicity in pharmaceuticals and food products.

Funding: Development of globally pioneering toxicity test method required for new chemical regulations for petroleum refinery substances and other substances (Development of techniques for testing hepatotoxicity, nephrotoxicity, and neurotoxicity in vitro) for the Ministry of Economy, Trade and Industry (FY 2011-2015)

🔑 Bio-pharmaceutical Development

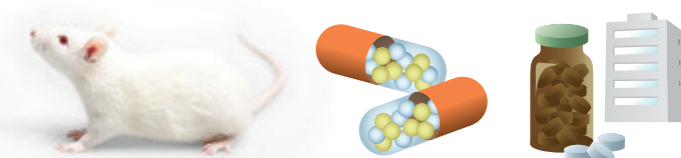
Complete human antibody-producing rats

We are creating rats that contain MAC vectors with entire human antibody genes in order to efficiently create effective bio-pharmaceuticals.

Funding: Basic Science and Platform Technology Program for Innovative Biological Medicine, Ministry of Education, Culture, Sports, Science and Technology(MEXT) / Japan Agency for Medical Research and Development (AMED) (FY 2014-2018)

High-yield antibody- or protein-producing cells

Artificial chromosome vectors can be used to greatly boost the long-term, stable expression of target genes in cells that are resistant to silencing. These cells offer a much higher yield of proteins with less variable quality between clones obtained than in the past.



Use in genetic and regenerative medicine research and in functionality assessment of pharmaceuticals and food products

Professor Mitsuo Oshimura

- Specially Appointed Professor, Chromosome Engineering Research Center Tottori University
- Director-General of Research, Bio Frontier Office, Tottori Industrial Promotion Organization
- Executive Director, Tottori Bioscience Organization
- Chief Executive Officer, Trans Chromosomics Inc.

Appointed Professor, Department of Life Sciences, Faculty of Medicine, Tottori University, after working at the New York State Roswell Park Cancer Institute, Tokyo Medical and Dental University, and Kanagawa Cancer Center. He also served as Project Leader in the 21st Century Center of Excellence Program funded by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and as Director of the Chromosome Engineering Research Center. He currently holds the positions of Project Director in the regional innovation business, Specially Appointed Professor at the Chromosome Engineering Research Center, Tottori University and Chief Executive Officer of Trans Chromosomics Inc.; he is a leader in pursuing Tottori University's goal of "Fusion of Knowledge and Practice" and Tottori Prefecture's "Economic Regeneration and Growth Strategy", to establish the Western Tottori Bio-cluster around Yonago City.

The bioindustry is a foundation for the implementation of "Medical Care Innovation Strategy", one of several economic revitalization and growth strategies set up by Tottori Prefecture, and chromosome medical engineering technology developed by Tottori University is the driving force of the industry. Here, we interviewed Professor Mitsuo Oshimura (Professor Emeritus, Tottori University), who is an inventor of chromosome medical engineering technology, and Professor Yoshiji Fujita, who is Strategy Director of MEXT's chromosome medical engineering project, on the prospects of the bioindustry in Tottori Prefecture.

Could you tell us about the potentials of chromosome medical engineering technology

Fujita: It may be easier to explain the reason why I was interested in the technology developed by Prof. Oshimura. Consider how mobile phones and smartphones have changed the world. You can hardly find payphones and disposable cameras now in towns and cities. News has become readily accessible. Technologies in the world have changed accordingly. When I came across the antibody production technology developed by Prof. Oshimura, I thought to myself "chromosomes can



A dialogue between the research and development leader and the business strategy leader

Bio Industry and Regional Revitalization

change the world". I sensed this based on my experience in pharmaceutical companies for many years. I acquired the ability to identify true excellence. It is easy to imagine that the market capitalization of Trans Chromosomics Inc. will jump to the top or second highest in Tottori if the company were to make an initial public offering (IPO) in a few years. It is not difficult to predict because the path is simple up until that point. The challenge would be how the company envisions its expansion after that. How technology can change medical care need not be considered. The next step for artificial chromosome technology is entering the field of regenerative medicine; treating conditions that are untreatable with current medicine. The company will need to take action to achieve its full potential after the IPO, which will be made in a few years. I am confident that chromosome engineering technology can fundamentally change health care including pharmaceuticals, and that the company's business will grow to a scale similar to that of bigger companies.

It seems that human antibody-producing mice developed by Kyowa Hakko Kirin Co., Ltd. is the start point of commercialization of chromosome medical engineering and business setup.

Oshimura: Money was not the focus when we were young researchers, but now, we have to think about giving back to the community. After meeting Prof. Fujita, I realized that my basic research could really be put to practi-

cal use. My feelings regarding social contributions through my basic research have become stronger and stronger.

Fujita: In such endeavors, the most important requirement is estimation of the value of the technology. With that said, the value of negotiations with a major pharmaceutical company would be two orders of magnitude higher than what Prof. Oshimura imagined. Universities seem to make million-yen business deals, but you cannot start a business that way. Our aim should be billion-yen deals (collectively, a ten billion-yen deal); otherwise, it will not lead to true industrial growth. If you can bring several companies into such large-scale business, industry will grow spontaneously.

Are there any particular organizations and personnel required for industrial growth?

Oshimura: We need to consider how the region can be vitalized, and how to keep human resources within the area, not centralized in big cities. Labor is essential to achieve this dream, and "passion", if expressed in one word, is crucial. This requires a desire to achieve clear goals in the region and an entrepreneurial spirit, instead of an attitude of seeking job stability with a big company. Showing young researchers how to set up business is very important, but Japan is not making effort to develop such talent. Of course, basic research is important, but universities should provide students with opportunities to learn about how research can contribute to society, otherwise they will not survive.

Fujita: Take Cambridge University, for example. About five ventures are established there in one week. Also, scientists do not leave the area, mainly because many other positions are available. So, they can think, "I'll go elsewhere if this doesn't go well". In Cambridge, several tens of thousands of people are employed by venture companies alone. If family members are counted, the size there will be similar to that of Yonago City. I think that this is one of the directions that Yonago should aim for. People tend to stay with big companies even though conditions are exploitative; they do this out of fear of losing their livelihood. I would like to change the system slightly to integrate dreams into it. The success of Trans Chromosomics Inc. would help such people, and that would be a vital contribution of Prof. Oshimura to society, and this is his ambition. It is easy to expand the company. It is possible to establish overseas branches, if you wish. But the basis is having conditions where people can earn their livelihood while taking on interesting responsibilities. True venture companies ensure a profit for another 10 years, or even for 15 years, and then, inform investors that the companies will use investors' money to achieve the next dream. I can see the potential in the company led by Prof. Oshimura, and that is why I work with him.

There are several university spin-offs within Tottori Bio Frontier...

Oshimura: I constantly think of how my basic research can be integrated into society, thereby making a solid contribution. People say technology is

the foundation. I have a technology that can compete worldwide, and I believe that this is my absolute strength. So, what matters now is how to sell it. And what I am looking for now is, as Prof. Fujita mentioned earlier, local young people who live in the region and are eager to vitalize the region.

Fujita: Firstly, finding personnel full of spirit and drive is essential.

Oshimura: Then, a successful example and a person who can take the leadership role are necessary.

Fujita: Yes, that's right. For example, once Trans Chromosomics Inc. becomes one of Tottori's leading listed company, supporting companies or businesses will be formed spontaneously. I would like to show a good example of expansion. And I believe that the ambition to give back to the community, and passion to contribute to Yonago City and beyond within Tottori Prefecture be always kept in mind.

Oshimura: I would like to invent something that people can gather around. For another 10 years, I will try to make



Professor Yoshiji Fujita

- Visiting Professor, Chromosome Engineering Research Center, Tottori University
- Specially Appointed Professor, Advanced Clinical Research Center, Fukushima Medical University
- Specially Appointed Professor, Graduate School of Industrial Science and Technology, Tokyo University of Science
- Strategy Director, Regional Innovation Strategy Support Program (MEXT)

Previously worked for Upjohn Tsukuba Research Center, Glaxo Japan K.K. (Board Member, and Director of the Tsukuba Research Center), GlaxoSmithKline K.K. (Vice President of Research and Development), Sheffield University (UK, Visiting Professor) and Tsukuba University (Visiting Professor). He is currently involved in venture business support at Tokyo University of Science, Tottori University, and Fukushima Medical University. Within Tottori Bio Frontier, he is committed to promoting commercialization of chromosome engineering technologies as Strategy Director, Regional Innovation Strategy Support Program.

it so that this company has globally competitive, totally innovative technology; otherwise it will lose the game.

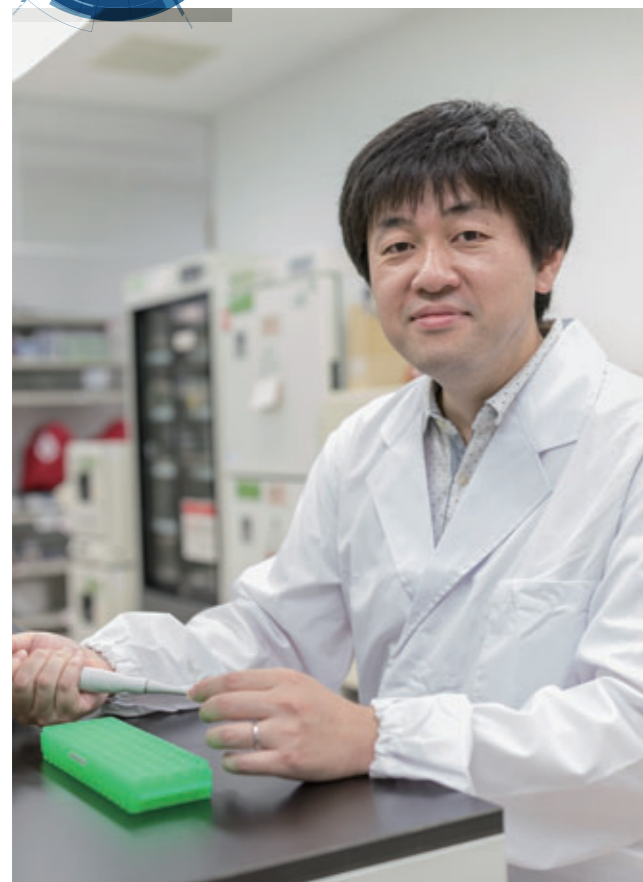
Fujita: If there is a successful example and all obstacles are easily overcome, many others will follow suit. However, if obstacles are difficult to overcome, nobody can enter the same field. This is what you must aim for. If you are confident in your technology that is advanced at least 5 or 10 years ahead, even for major pharmaceutical companies, you are in a very strong position. You must create the situation such that those companies wish to come to the region, rather than you inviting them to the region. The local government's goal will be "attracting companies to the region" either way, but I recommend that you be proud of your technology and have a "come here or miss out" attitude.

Oshimura: I must work hard then, and I sincerely hope to achieve such a big dream. I have always believed that if you have a dream, it will come true, so I'd like young people to have big dreams, and believe that they are heading toward the dream. The dream can be big; don't worry about failure.



Seiji Yamauchi

Chief Researcher, Research and Development Division, chromocenter Inc.



the field of regenerative medicine is based on our post-gene transfer chromosome analysis and chromosomal abnormality analysis, respectively. Cultured animal cells need to be evaluated as to whether they retain their original clonality during long-term cell culture. Our proprietary artificial chromosome vector technology is applicable in diverse fields, and this is our advantage.

— Our future vision: development of overseas business

One of the guiding principles of our company president is "business expands beyond Japan", and thus the company aims to establish a basis to set up an overseas company within the next five years. To realize this vision, it is essential to foster talent for global business development and proactive cooperation with advantageous companies in overseas development. Biotechnology has various subspecialties, many of which could employ the use of artificial chromosome vectors. As a bio-venture, we keep moving and challenging new ground. We expect novel business development, including overseas locations, within a few years.

— City infrastructure facilitating bio-industry settlement

Research facilities and centers must be secured for development of the bio-industry. However, there is no facility like Tottori Bio Frontier within the prefecture. Furthermore, the bio-industry is still a new frontier for Yonago City and Tottori Prefecture. Research-related positions are rare in Tottori Prefecture, even if one aspires to such a position. chromocenter Inc., hopes to become an attractive employer of such individuals. Fostering local understanding and government support is essential for expanding business centers and raising recognition of the bio-industry, so we are conducting public relations activities to raise awareness of our business and proprietary technologies. This has resulted in recruitment of talent in various fields, from inside and outside the prefecture.

The success of our current research will reduce costs of currently expensive biopharmaceuticals, and offer cost-effective therapeutic options to patients. Regarding cell evaluation technology, we aim to contribute to safety index-setting in cell therapy. Several ventures have been established within the group as spin-offs from research led by Prof. Oshimura. As a group, we would like to collaborate using individual expertise for development of the bio-industry in Tottori.

— Diverse collaboration using our proprietary "artificial chromosome vector" technology

The chromocenter Inc. constructs protein-producing cell lines and evaluates cells. Our proprietary artificial chromosome vector technology is our greatest asset. We work with several client companies to construct and evaluate protein-producing cells and to evaluate cells provided by clients. Our proprietary artificial chromosome vectors were created from intracellular structures (chromosomes), and the technology can be applied to chromosome analysis. Numerous clients in various fields trust in our cell safety assessment and gene transfer assessment of chromosomes. Our close working relationship with clients involved in protein production as well as with those in



Business activities

We focus on performance improvements for biopharmaceutical-producing cells (CHO cells) and quality assurance of various types of cells, including iPS cells, ES cells, and material-producing cells.

Company name chromocenter Inc.
CEO Takashi Matsuoka
Capital 163,714,000 yen
Established June 15, 2005
Location 133-2 Nishi-cho, Yonago, Tottori
URL <http://chromocenter.com/>



Tadashi Nishida

President, GPC Laboratory Co. Ltd.



the element of "glowing" using our advanced technology and expertise acquired through collaborations with the National Institute of Advanced Industrial Science and Technology (AIST) and several universities.

Previously, fluorescence was commonly associated with green color, and luminescence with fireflies. But now, many types of luminescent and fluorescent labeling are available to track gene movements.

However, it is difficult to transfer multiple genes into cells and animals. The technology developed by Professor Oshimura (Tottori University) enables easier transfer of multiple genes to cells. We sensed a real market need for the technology to detect multiple luminescent-labeled targets, and subsequently achieved success visualization of vital phenomena using combined technologies developed by AIST and Tottori University.

Our strength is not limited to the above three technologies. We are aware of continuous advancements in technology and flexibly incorporate this to enhance our product development capability.

— Becoming a leading drug discovery company

We currently offer the solution, luminescent/fluorescent imaging cells or animals, to solve the problem of clients. In the future, we will use our acquired expertise to enter the drug discovery business, and hopefully, become a leading company in this field. For example, we would like to build a complementary relationship with a company that has a compound library but does not have evaluation system or animal experiments expertise.

Drug discovery is area of active research. We cannot expect the company to grow if we have ordinary business offerings or an ordinary way of doing business. We engage in "evaluation of pharmaceuticals" and "detection of disease" using luminescent and fluorescent imaging technologies, and this characteristic approach will create a new evaluation mechanism that depicts pathology and vital phenomena from a unique angle, ultimately resulting in company growth.

To achieve this, we are seeking highly motivated individuals with potent ideas to pursue interesting business development together.

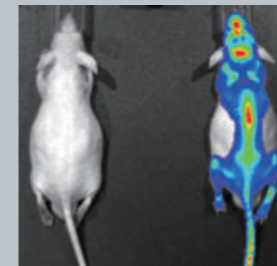
To attract of numerous biotechnology companies to this region, we hope that we can access stronger and expanded support (such as research funding and intellectual property strategies), in addition to support to securing of researchers and engineers within the region.

— Glowing cells! Glowing mice! Offering Luminescent and Fluorescent Imaging Technologies

Our business focus is visualization of drug efficacy and physiological phenomenon. We utilize luminescent mechanism derived from marine life and lighting bugs to generate glowing cells and animals for evaluation of pharmaceuticals and functional components.

Our three main strengths are luminescence/fluorescence imaging technology, chromosome engineering-based genetic modification, and generation of genetically modified animals. We fuse these three technologies to generate glowing cells and animals.

The technology of generation of genetically modified cells and animals has become common in drug discovery, to which we add



Business activities

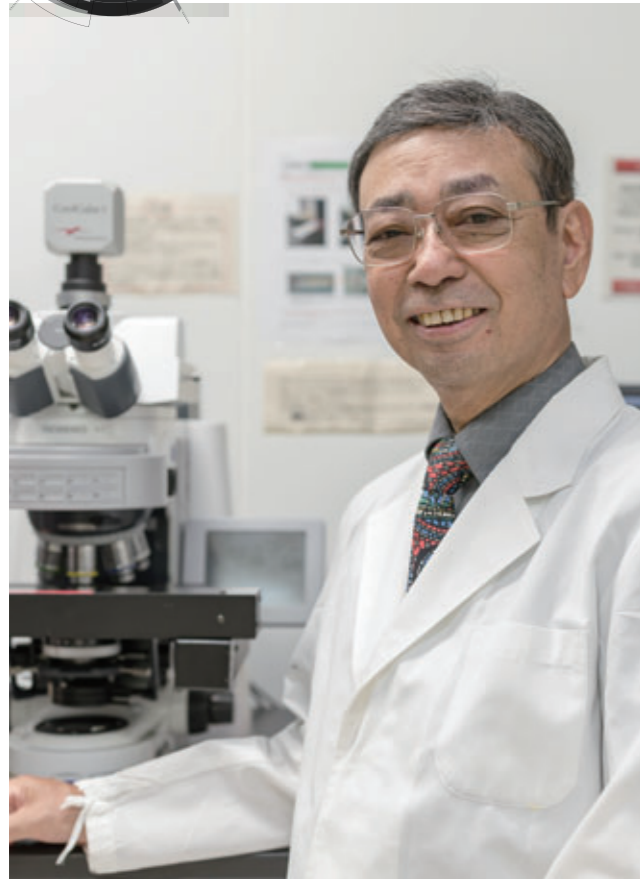
GPC laboratory generates unique luminescent and fluorescent imaging tools for visualization of the efficacy, toxicity, and safety of compounds, as well as visualization of various physiological phenomena and diseases. We contribute to the development of pharmaceuticals, health-promoting foods, and dietary supplements through creating and providing these imaging tools.
●Generation of genetically modified cells and animals
●Sales of cell lines and experimental animals
●Evaluation of innovative medical supplies and functional food ingredients

Company name GPC laboratory Co. Ltd.
President Tadashi Nishida
Capital 2.1 million yen
Established March 8, 2012
Location 86 Nishi-cho, Yonago, Tottori
URL <http://www.gpc-lab.co.jp/>



Mitsuo Oshimura

CEO, Trans Chromosomics, Inc.



Globally competitive technology is key

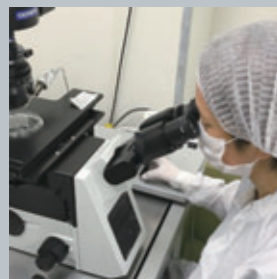
The most important asset in bio-venture operations is globally competitive technology. Then, you need to think about how you can use that in business development. Marketing, business planning and negotiation skills are also essential. Without building a win-win relationship, business will not be established. Research scientists must diligently strive to accumulate technologies, but that is not enough. Our business is about to get on the right path through cooperation with entrepreneurs and business personnel who share our passion. Money is a means to turn your passion into something real. It is important that the same goal, namely, "contribution to the society" be shared by research scientists and businesspeople. As in the case of finding a complementary partner, "interpersonal encounters" and "combination" are important. The company aims to form a team wherein the right people are put in the right place. If we encounter people who want to establish bio-ventures in Yonago City and the western region of Tottori Prefecture in the process of business development, we would be very happy to work with them.

To become a center of sustainable business creation

We aim to become a leading globally competitive company and a center of sustainable business creation, enabling the establishment of a stream of ventures. Our initial focus has been on creation of humanized animals and the ensuing drug discovery, but for future growth, the business should keep up with the times, adapting to the changing needs of the society. First, we must have clear visions, and then fuse these well with foresights extending to the outside world. It is important to continuously create products that satisfy the demands of the times. Human resources are absolutely essential to achieve this, and so we seek research scientists who share our passion and are committed to achieving success in Yonago. Those who have the technical skills to compete on a global level are particularly welcome. Administrative and regional support/understanding are also essential for us to be a center of sustainable business creation, as well as for firm establishment of bio-industry in the region. For example, growth of the bio-industry across the region requires land for setting up research facilities and offices. Tottori Prefecture has included the bio-industry in the "Economic Regeneration and Growth Strategy", and we welcome similar support from Yonago City. Our ultimate aspiration is to establish a large bio-cluster in Yonago City and the surrounding areas.

Culmination of over 40 years of chromosome research

As the company name implies ("trans" denotes transfer, and "chromosomic" of the chromosome), our business is based on chromosome transfer. We create partially humanized mouse or rat models (such as human antibody-producing animals and animal models of Down syndrome) and offer these to pharmaceutical companies for collaborative development of human therapies. Chromosomes were my theme when I started my career in research. My research in an academic setting resulted in development of many patented technologies with which chromosomes can be freely manipulated. In a bid to establish a business to demonstrate the impact of my basic research on the society, I set up Trans Chromosomics Inc., which is the culmination of my research of over 40 years.



Business activities

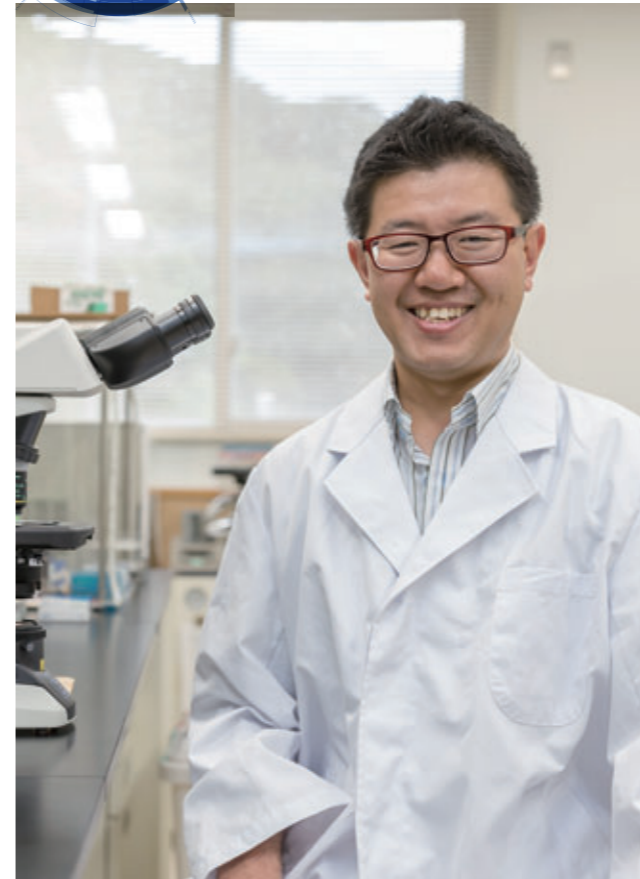
- Development, contract development, and sales of pharmaceuticals and other agents
- Chromosome engineering-based development of pharmaceuticals and other agents
- Mouse and rat that produce fully human antibodies and development of therapeutic antibodies
- Development of rat and mouse models of rare hereditary diseases
- Development of humanized mice and rats
- Contract chromosome analysis, contract creation of engineered cells, etc.

Company name Trans Chromosomics, Inc.
 CEO Mitsuo Oshimura
 Capital 111 million yen
 Established December 17, 2014
 Location 86 Nishi-cho, Yonago, Tottori
 URL <http://trans-chromo.wixsite.com/trans-chromosomics/>



Yasuhiro Kazuki

CEO, PACT, Inc.



certain antibodies in dogs which were initially developed for humans and modified for use in dogs. We intend to out-license to veterinary pharmaceutical companies as soon as the therapeutic effects are proven. We oversee the genetic modification of human therapeutic antibodies for use in dogs, and verification of the therapeutic effect in animals; the above-mentioned organizations in Tottori University conduct research and provide us with technical advice. After achieving financial sufficiency through business using such therapeutic antibodies, we will proceed to the second phase with a focus on cell therapy. Various forms of cell therapy for intractable diseases (such as muscular dystrophy) are available at the Chromosome Engineering Research Center, Tottori University. Furthermore, we also have a vision of cell therapy for intractable diseases in dogs that can be translated to clinical research in humans.

Vitalizing the region and boosting employment quickly

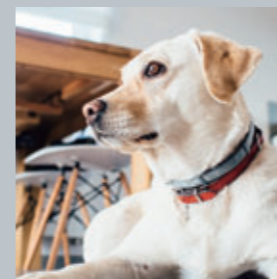
The key to success is out-licensing of therapeutic antibody. We expect to achieve this relatively quickly, perhaps within 5 years, rather than 10 or 20 years. When our finances are boosted by out-licensing, we would solicit a big pharmaceutical company as a mergers and acquisitions (M&A) partner to set up a subsidiary of the company in Yonago, thereby vitalizing the Yonago/Tottori region and boosting employment.

Advancing with passionate individuals who have a stake in the company

We seek all-rounders, who are interested in marketing and business, as well as research, and who are thoroughly passionate about this company. I am an academic faculty member as well, and believe that encouraging students to develop a spirit of entrepreneurship and a desire to become an entrepreneur is part of education. Nevertheless, Tokyo is still considered the business hub of Japan, and thus inviting excellent research scientist with industry experience and entrepreneurial/business mindset to a region such as ours is challenging. A possible solution to this would be government measures encouraging an intra-regional approach where "Things that can only be done within the region should be done in the region". Our success is important to demonstrate the entire process from drug discovery to out-licensing, and then to M&A and an initial public offering. We will show that bioindustry in local regions is achievable and not just a fantasy. We will be then able to recruit talented individuals who wish to be involved in research while living in regions outside of big cities. Ventures need to have vision and philosophy, and mine are "to treat cancer" and "to vitalize the region". We would like to fulfill this vision with team players who share our aspirations.

Treatment of refractory diseases in companion animals

PACT Inc. mainly develops therapeutic agents and therapeutics for diseases in companion animals, with emphasis on the development of therapeutic antibodies and cell therapies. The company is the first joint-venture comprising three organizations in Tottori University: Department of Veterinary Medicine, Faculty of Agriculture; Chromosome Engineering Research Center; and the Faculty of Medicine. We harness the expertise of each organization in developing business, this being our strongest advantage. Another advantage is our strong association with Trans Chromosomics Inc., which is also a venture spin-off from Tottori University. Human-use pharmaceuticals, developed by Trans Chromosomics Inc., will be used to develop agents for treatment of diseases in companion animals. Our goal is the developing treatments for refractory diseases in companion animals, such as antibodies for anti-cancer therapy in dogs. We are currently evaluating the therapeutic effect of



Business activities

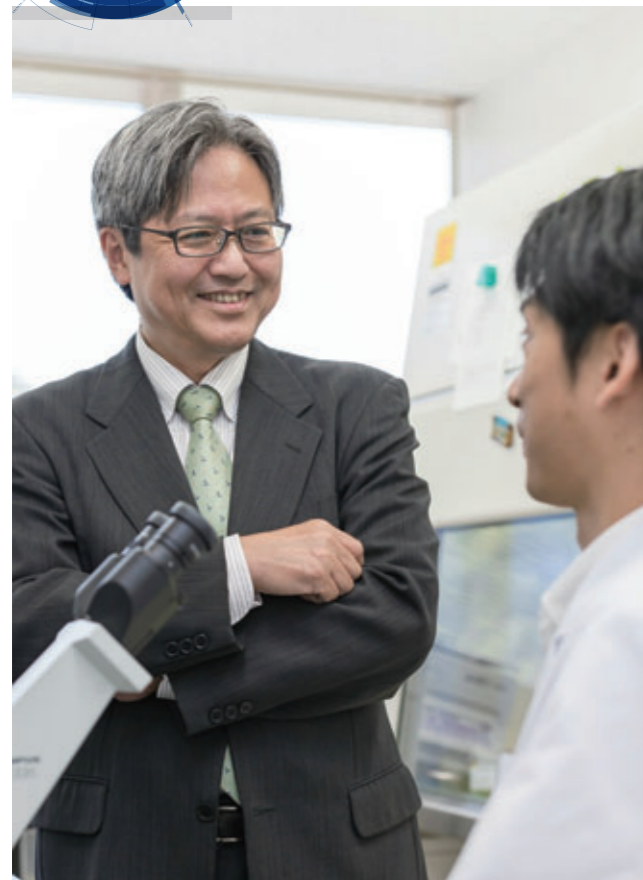
- Research and development of therapeutic agents for companion animals; research and development of cell-based, genetic, and regenerative medicine; and manufacturing and sales of those products
- Development and sales of antibodies for cancer therapy in companion animals
- Construction and contract construction of animal disease-related databases

Company name PACT, Inc.
 CEO Yasuhiro Kazuki
 Capital 16.5 million yen
 Established February 10, 2017
 Location 86 Nishi-cho, Yonago, Tottori
 URL <http://tottori-pact.wixsite.com/mysite/>



Makoto Kitaura

Ph.D., Director, Corporate Planning/
Technology Training Institute/Cell Technology, KAC Co., Ltd.



Tottori University intellectual property to make them available to researchers. So, in a way, we are also a startup in Yonago. Because we utilize Tottori University's intellectual property, we have managed to receive funding from Tottori Prefecture. Having a base in Bio Frontier is advantageous because it allows for close daily communication about our research with Tottori University-based research scientists, which accelerates new product development. In addition, we have free access to advanced and expensive instruments that small and medium-sized companies cannot usually access. The research and development environment here is excellent.

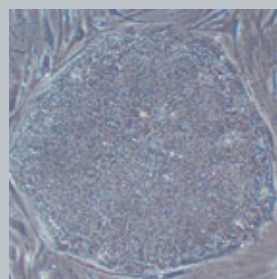
— Production of glowing hepatocytes based on Tottori University research and licensed induced pluripotent stem cells

Three products are mainly produced here in Yonago, all of which are in alliance with other companies/organizations. The first is a fluorescent hepatocyte line CYP3A4G/7R HepaRG, in which a certain gene was introduced into HepaRG cells with human hepatocyte characteristics (BIOPREDIC International, France) using technology developed at Tottori University, thereby enabling fluorescent monitoring of cell differentiation status. The second is human induced pluripotent stem cells (iPS) cells, for which research Professor Yamanaka of Kyoto University was awarded the 2012 Nobel Prize in Physiology or Medicine. We have a license from iPS Academia Japan. We obtain tissue and blood specimens from healthy individuals and patients after informed consent through overseas partner companies, and we produce iPS cells from these specimens in Yonago. The third is the transporter protein-expressing PREDICELL. Transporter proteins play an important role in pharmacokinetics, and thus PREDICELL is extremely useful in research on drug-drug interactions. We are the only Japanese manufacturer and seller with a license from SOLVO Biotechnology (Hungary). Products made in Yonago are ready to use in experiments, and lengthy culture by users, which is usually required before start of such experiments, is not necessary.

As described above, Yonago is an important base for our new business involving new cell development and manufacturing. In addition to our close working relationship with Tottori University, cooperation with local industries, the business community, and a financial institution is necessary for development of our fully independent business in the Yonago/Tottori area.

— Development and manufacturing of cell products using Tottori University's intellectual property

KAC Co., Ltd. is not a university spin-off. It is a Kansai-based company, with a 40-year history of contract breeding and maintenance of experimental animals. In addition to this initial business focus, the company has two more core businesses, contract testing using experimental animals with production of genetically modified animals and provision of imported cells and tissues for research use. We had an opportunity to conduct collaborative research with Tottori University a few years ago, and that led to our becoming a tenant of Bio Frontier offices to set up our Cell Technology Laboratory. Here, we started creation and production of cells with novel characteristics using



Business activities

- Contract maintenance of experimental animals, dispatch of technicians, and consulting
- Contract research (animal experiments, production of genetically modified animals, breeding and maintenance of experimental animals, etc.)
- Sales of biological materials and reagents for research (such as cells, tissues, reagents etc.)
- Contract research and production related to regenerative medicine and iPS cells
- Sales of materials and devices for experimental animal care, sterilization service for animal care facilities etc.

Company name KAC Co., Ltd.
 CEO Satoru Kitamura
 Capital 35.625 million yen
 Established November 1, 1978
 Location 40 Nishinokyo Nishigekko-cho, Nakagyo-ku, Kyoto City, Kyoto
 Tottori-Cell laboratory: Tottori Bio Frontier Rooms 301 and 313, 86 Nishi-cho, Yonago, Tottori
 URL <http://www.kacnet.co.jp/>



Yuji Arimatsu

Group Leader, Tottori Research Center,
TechnoPro, Inc. TechnoPro R&D, Co.



second laboratory, and we work together with clients to satisfy their requirements for knowledge, facilities, and expertise. We make concerted effort to offer clients solid support in their product development.

— High demand for screening in drug discovery

We started a new contract research service, screening for drug discovery, in Yonago. Tottori Bio Frontier was very supportive and provided us with a foundation in the early stages. We started this business in Yonago with prospects of future collaboration with bio-companies using chromosome engineering technology, which is an active research focus in Tottori University.

Our main service here is to establish assay systems, assisting clients to perform screening of libraries of compounds. Our clients are currently located all over Japan, and we expect overseas clients in the future. As a contract research organization, we must execute required experiments, and so a trusting relationship with clients is essential.

Thus, we are looking for individuals who with incentive and initiative. Our current research staff is experienced in various fields, but also have occasion to be involved in research activities outside their expertise. Our human resource development is mainly through on-the-job training. We are looking for personnel willing to take on a challenge outside their specialty, thereby expanding their range of expertise.

— Contract research uniquely tailored to individual clients

Contract bio-research is our main business here in Yonago, and our diverse clients include pharmaceutical companies, biotechnology-related companies, chemical companies, and university-based research teams across Japan. We can accommodate research in various fields, including genetic engineering, cell engineering, protein engineering, animal experiments, and analysis.

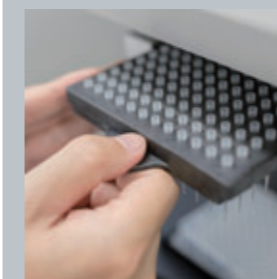
A clear difference between our service and common contract research is that we collaborate with clients from the stage of experimental design so that the research is tailored to individual clients needs, instead of simply handing in research outcomes to clients. In other words, our laboratory serves as clients'

— Aiming for the "first drug discovery in Tottori"

At Tottori Bio Frontier, we would like to expand our screening business in the field of drug discovery. We seek to be equipped with as many high-throughput screening instruments as possible so that we can take on any screening requests.

Also, we envision becoming an industry standard for creating screening assay systems.

Chromosome technology is the core of Tottori Bio Frontier and business development using this technology is our goal. We believe that raising awareness of the benefits of chromosome engineering and establishing systems for disseminating this technology will result in future development of bio-industry.



Business activities

- Research and development focused on chemistry and biotechnology, and clinical development in the field of pharmaceuticals

Company name TechnoPro, Inc. TechnoPro R&D, Co.
 CEO Masami Hayafune
 Capital 100 million yen (TechnoPro Holdings, Inc.)
 Established October 1988
 Location Roppongi Hills Mori Tower 35F, 6-10-1 Roppongi, Minato-ku, Tokyo
 Tottori Research Center: 86 Nishi-cho, Yonago, Tottori
 URL <http://www.technopro.com/rd/>

Hub Management

Management and Operation of Hub Facilities

Manages and operates Tottori Bio Frontier facilities
 ◎Office ◎Laboratory ◎Animal maintenance room, etc.

Promotes use of accessible experimental equipment
 ◎Reasonable usage fees for users to reduce financial burden
 ◎Staffing to support users for experimental equipment

Ensures biosafety in animal experiments and maintenance in compliance with the Cartagena Protocol and the Act on Welfare and Management of Animals
 ◎Placement of "Chief Safety Officer" and "Animal Experiment Manager"
 ◎Operation of the safety committees for genetic engineering and animal experiments

Leads and coordinates cooperation among industry, academia, government, and related organizations

Commercialization support

Offering Comprehensive Support to Users

Promotes commercialization by industry-academic-government cooperation
 ◎Holding business operation committees etc. as a management organization
 ◎Facilitation of business collaboration via participating in meetings and exhibitions
 ◎Promotion of externally funded commercialization
 ◎Utilization of business setup menus provided by "Tottori Industrial Promotion Organization"

Coordinates commercialization by bio-specialist staffing
 ◎Director-general of research: provides advice and suggestions for advancing research and development
 ◎R&D coordinator: visits bio-companies and provides updates on relevant trends
 ◎Bio-manager: provides support for commercialization

Human Resource Development

Nurturing Human Resources in Biotechnology

Implements biotechnology training on the basis of industry-academic-government cooperation
 ◎Training of professional technicians with system/machine operation hands-on training
 ◎Seminars for deeply understanding of chromosome medical engineering
 ◎Business seminars to foster entrepreneurial spirit
 ◎Training of laboratory animal technicians
 ◎Well-developed lecture courses cooperated with Tottori University

List of instruments

- | Storage equipment | General equipment | |
|--|---|--|
| <ul style="list-style-type: none"> ● CO2 incubator ● Large cooling incubator shaker ● Small cooling incubator shaker ● E.coli culture incubator ● Dry heat sterilizer ● Paraffin melting unit ● Liquid nitrogen tank for cell preservation ● Ultra-low temperature freezer A ● Ultra-low temperature freezer B ● Cold storage showcase medicated ● Medicated cold storage warehouse ● Chemicals refrigerator | <ul style="list-style-type: none"> ● Clean bench ● Inverted biological microscope (Inverted microscope for routine use) (Trinocular microscope) ● Swing-out refrigerated centrifuge ● Biosafety cabinet ● Autoclave ● Inverted fluorescent microscope ● All-in-one microscope ● High-performance centrifuge ● Electroporation system | <ul style="list-style-type: none"> ● Biological microscope with teaching head ● Stereomicroscope ● Compact refrigerated centrifuge ● Gel imaging device ● Microvolume spectrophotometer ● Spectrophotometer ● PCR machine ● Automatic washing machine for laboratory equipment ● Open-sided L.R fume hood ● Super electroporator |

Accumulation of 'chromosome medical engineering technology' at Tottori Bio-Frontier.

3F chromosome medical engineering technology can be used to conduct animal experiments and gene recombination experiments aimed at creating new industries
 4 rental private rooms / 4 rental laboratory rooms / 4 animal rooms




 Animal room


 Laboratory room (rental type)


 Business meeting room


 Private room

2F Latest facilities for gene, cell and animal analyses
 Shared laboratory (open to academia and private companies)
 * Cell Laboratory * Instrumental analysis room * Genetics Laboratory




 Cell laboratory


 Instrumental analysis room


 Genetics laboratory

1F Consolidated Tottori University's 'Chromosome medical Engineering Technologies'
 Tottori University Chromosome Engineering Research Center (Open laboratory and laboratory rooms (shared type)) and training room




 Training room


 Open laboratory


 1F Laboratory room (shared type)

- | Specialized equipment | | |
|---|---|---|
| <ul style="list-style-type: none"> ● Incubator microscope ● Cell analyzer ● Time-lapse bioluminescence analyzer (Light-emitting live-cell imaging system) (Incubated cell real-time luminometer) ● Microplatereader ● High-sensitivity cooling CCD camera ● Ultracentrifuge ● Chemiluminescence and fluorescence imager ● Multi-sample pulverizer ● Ultrasonic pulverizer(homogenizer) | <ul style="list-style-type: none"> ● Ultrasonic pulverizer(cell disruption equipment) ● Real-time PCR ● Gene isolation system ● Confocal microscope ● Microscope for chromosomal analysis ● Microdissection ● Bio-sample pulverizer ● Animal tissue fixation device ● Automatic airtight fixation and embedding device ● Paraffin-embedded block ● Microtome | <ul style="list-style-type: none"> ● Paraffin stretching unit ● Cryostat for infection prevention and control ● Blood biochemical analyzer ● Fully automated rotary microtome (suitable for resin-embedded specimens) ● Program freezer ● Small animal anesthesia machine |