Enzyme Wave 2016

Volume 19

Courtesy of Toyota Motor Corporation

Innovation Create the future with technology

AMANO Amano Enzyme

Enzyme Wave vol.19

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MIRAI

Courtesy of Toyota Motor Corporation

Information

The Prof. Jokichi Takamine Research Foundation, Activity News

Professor Jokichi Takamine

Living in the turbulent times of the late 19th and early 20th centuries, Jokichi Takamine left his mark not only as a scientist and entrepreneur but also in international diplomacy. He is known as the father of modern biotechnology due to his research and development of microbially-derived starch degrading enzymes centered around Takadiastase.

Dr. Jokichi Takamine
(photo courtesy Great People of Kanazawa Memorial Museum)

The Jokichi Takamine Research Foundation, specified nonprofit corporation

The Prof. Jokichi Takamine Research Foundation conducts activities to make Professor Takamine's achievements and successes more widely known, such as by publishing a journal, giving lectures, sharing information, and so on.

Lecture at Takaoka Municipal Junior High School

Lecture at Kanazawa Institute of Technology

Major Past Activities

In September 2015, Takadiastase was added to the National Museum of Nature and Science's list of Essential Historical Materials for Science and Technologies (popularly called Future Engineering Heritages). 121 years after the related patents came into effect, the enzyme is back in the spotlight.

Future Engineering Heritages Award
Photo: Daiichi-Sankyo Co., Ltd.

It has also been decided to include information about Professor Takamine in a MEXT-approved textbook (for health and physical education at junior high schools). We have produced a scientific and biographical manga (not for general sale, only available for members) to generate interest within an even wider age group. We will continue to devote ourselves to such activities in future.

Scientific and biographical manga

Recruitment of new members

Our research foundation widely recruits people who agree with our goals. All members receive publications related to Professor Takamine and a regularly issued journal, along with invitations to various talks and events and other newly obtained information. If you would like to join, please apply by letter including your name (in the case of corporations, your company name and department name), address with postcode, telephone number (landline only), profession, age and gender. We will reply with a payment slip for your initial membership fee and annual membership fee.

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*For further details (in Japanese), visit our website:
http://www.npo-takamine.org/ask.html

Column

The appeal of the Mirai FCV, toward the creation of the hydrogen society

Courtesy of Toyota Motor Corporation

Automobiles have brought people freedom of movement and contributed to our economic, social and cultural development. At the same time, amid concerns about climate change, environmental pollution, and the depletion of oil and other fossil fuels, the way we use energy and automobiles is being questioned more than ever before.

Recently, hydrogen is attracting a great deal of attention as a promising energy form for the next generation. A feature of hydrogen is its abundance (it can be made from sewage sludge, or even from water by using sunlight or wind power) and the fact that it does not generate CO_2 when used. Because it has a higher energy density and is easier to store and transport than electricity (batteries), hydrogen can cope with the variability and instability that are challenges for natural energies. Toyota believes that hydrogen will be the Potential energy of the future, and has been working to develop a fuel cell vehicle (FCV) for more than 20 years.

The mechanism of the FCV is to generate electricity in a fuel cell (FC) stack from a chemical reaction between hydrogen and oxygen taken from the air, and to use that electricity to power the motor that drives the vehicle. Unlike an internal combustion engine, the FCV generates electricity by a chemical reaction rather than burning hydrogen and is therefore highly energy efficient and has a short fuel filling time rather than a lengthy of charging time for a electric vehicle (EV). Characterized by producing only water and no substances of concern to the environment during driving, the FCV has the potential to be the ultimate eco-car that will contribute to the creation of a sustainable mobility society.

The development concept of the Mirai FCV is to be the “H_2 pioneer for the next century”. To enable a further 100 years of motoring, we have developed a vehicle aimed at pioneering the path to a hydrogen energy society.

With core Toyota technologies such as FC, we are particular about keeping technology within our grasp through internal development and production so that we can implement cost reductions and other engineering developments ourselves, and so we produce our fuel cells and hydrogen tanks in-house. We have achieved compactness and highperformance in both fuel cells and hydrogen tanks and, by introducing mass production and using less platinum, managed to cut system costs to one-twentieth of what they were in 2008. The Mirai's filling time of no more than three minutes and a driving range of approximately 650km (in JC08 mode; in-house measurement) put it on a par with gasoline vehicles in terms of convenience.

The progressive appearance of the Mirai is of great importance. We have aimed for a design that people can admire, so that residents of communities that lack infrastructure will think, "That's a cool car, I'd like to drive one. I wish our town had a hydrogen infrastructure too." By designing the exterior in such a way that shows its function of drawing in air (oxygen) and discharging water, we have aimed to make it instantly recognizable as an FCV.

We did not want to sacrifice any of the intrinsic "Fun-to-drive" feature just because this is an eco-car, and so we have paid extremely close attention to its drive, comfort and quietness, so that in a hundred years' time people will still think motoring is enjoyable. By installing the FC units near the middle of the car and under the floor, we have achieved a low center of gravity and a weight balance resembling that of a mid-engined car. We have also insisted on a rigid body, achieving a rigidity of about 160% that of TOYOTA FF (front drive cars). As well as the motor's responsiveness and high-torque acceleration, the finished car delivers good handling and a quiet, comfortable ride that will make people want to keep on driving it.

The car's name, Mirai, is the Japanese word for "future", and expresses our strong desire to open up the future of automobiles, the future of our children, and the future of the global environment. The innovation we aspire to in this car is not only innovation in mobility but also innovation toward the creation of the hydrogen society. The spread of FCVs and the realization of the hydrogen society is a long-term struggle that will take years and years. Needless to say, by further lowering our costs and improving performance, we will keep on striving to produce betters cars and facing the challenges of creating the hydrogen society. We sincerely hope that by supporting the Mirai we are taking the first firm step toward the realization of the hydrogen society.

Author Yoshikazu Tanaka

Joined Toyota Motor Corporation after completing his course at the Graduate School of Engineering, Kyoto University. After holding positions related to the development of new automatic transmission for the first-generation Vitz and multi-speed automatic transmission for rear wheel drive, he moved to the Product Planning Group in March 2006 to work on plug-in hybrid (PHV) development. From 2007 he was in charge of development of the Prius PHV as development leader, and since January 2012 has been chief engineer of hydrogen fuel-cell vehicle planning.

Report

Digestive enzyme formulas are recommended for the treatment of patients with functional dyspepsia.

Introduction

As the number of patients with Helicobacter pylori infection decreases, the percentage of functional dyspepsia patients who visit clinics with upper gastrointestinal (GI) symptoms but no gastric ulcers or gastritis by endoscopic examinations increases. Antacids such as histamine type 2 receptor antagonists or proton pump inhibitors or prokinetics, which improve gastrointestinal motility, are known to be less effective for most of the cases with functional dyspepsia (FD). It is believed that one of the reasons for the ineffectiveness of these agents for FD symptoms is that these patients show characteristic personality and they are often in a severe depressive mood when their symptoms are apparent

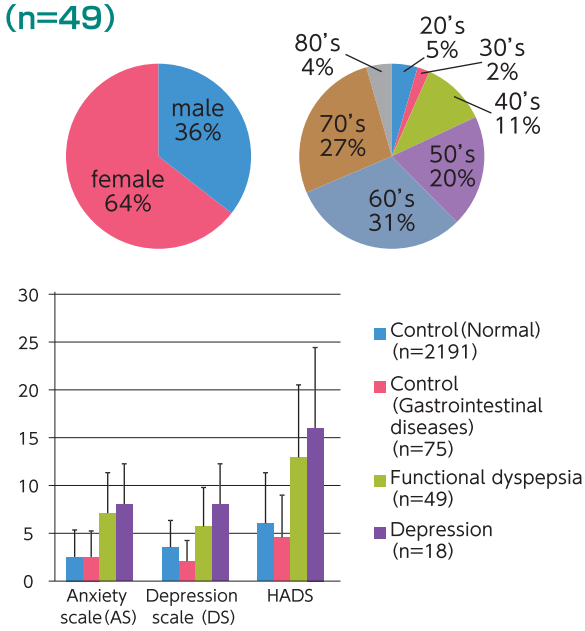
In a previous study, we have shown that digestive enzyme formulas are effective for both gastrointestinal symptoms and a depressive mood of FD patients when digestive enzyme formulas are given in combination with a dopamine type 2 receptor antagonist (Sulpiride), a potent agent which improves digestive tract motility. In this manuscript, a new therapeutic approach to patients with functional dyspepsia is described.

Most patients with FD suffer from symptoms related to anxieties or depressive mood

In a previous study performed in an European country, some populations in a community without visiting hospitals present both functional dyspepsia symptoms such as postprandial bloating or appetite loss and psychiatric symptoms such as an anxiety and a depressive mood. Therefore a strong correlation between these gastrointestinal symptoms and an anxiety or a depressive mood was proposed.

We conducted a questionnaire survey on employees working in a factory by the Hospital Anxiety Depression Scale (HADS) questionnaire designed to evaluate the anxiety or depressive moods of hospitalized patients. The questionnaires of 2,191 so called "apparently healthy" workers were analyzed. The HADS score of 13 and more is diagnosed as "depressive" by psychiatrists. Surprisingly, 12.1% of workers who are coming to work on every working day and not taking a sick leave by mental disorders feel depressed and had a HADS score of 13 or more. It was also shown that higher HADS scores are found in workers who subjectively feel pessimistic and also depressed. In addition, patients who are taking antidepressant had higher HADS scores. In other words, patients with FD have high HADS scores comparable to those of "patients with severe depressive mood" (Fig.1). Evaluations of subjective mood and subjective personality revealed an overlap of FD symptoms and anxiety/depressive moods.

Fig. 1 HADS scores of patients with FD



AS, anxiety scale; DS, depression scale; HADS, AS+DS

(Ko S et al. Gastroenterology 2012; 55:38-41)

Combined use of a dopamine D2 receptor antagonist and a digestive enzyme formula ameliorates functional dyspepsia symptoms

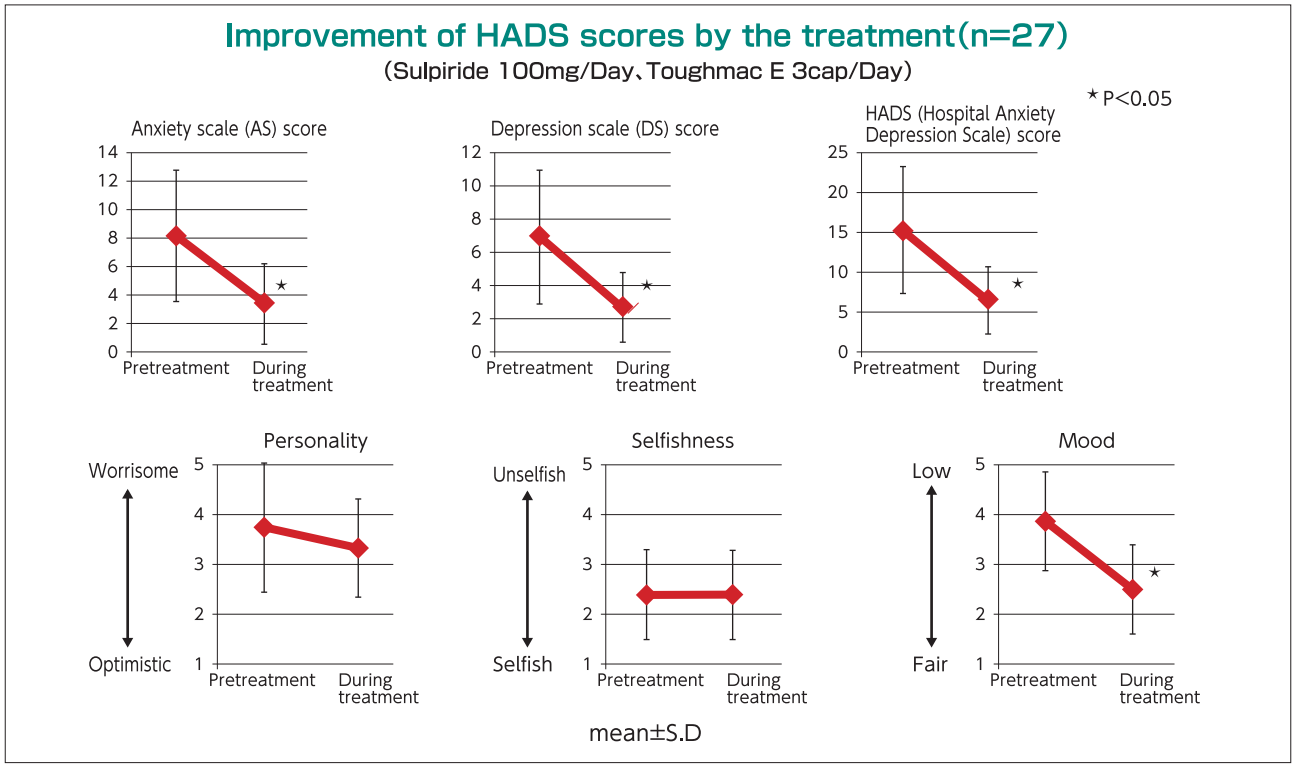
Antacids such as histamine H2 receptor antagonists or proton pump inhibitors are often prescribed to patients with symptoms such as a sensation of postprandial fullness or epigastric pain to suppress gastric acid secretion because these upper GI symptoms are believed to arise from hypersecretion of gastric acid. However, those agents are less effective to most of the patients complaining gastric symptoms. We have found that a combination regimen with digestive enzymes and Sulpiride, which is an agent effective for both digestive tract motility and a depressive mood at low doses, not only ameliorates GI symptoms but also decreases HADS score, improves depressive mood and even changes subjective personality of these patients (Fig. 2). Because each agent, digestive enzyme formulas and Sulpiride, has positive effect for

anorexia and mood disorders, it was not surprising that much stronger effect is found when two agents were given together.

Conclusion

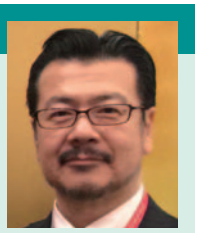
Digestive enzyme formulas are a combined agents that contains both animal digestive enzymes derived from porcine pancreas, pancreatin, and digestive enzymes derived from microorganisms. Different composition and digestive enzymes contained make each digestive enzyme formula unique. All Digestive enzyme formulas, except for one imported formula from Europe, are currently reasonably priced in Japan. They are safe and effective for general postprandial GI symptoms such as epigastric pain, bloating or anorexia. Given these advantages as GI treating agents, digestive enzyme formulas are strongly recommended as a regimen when patients complain wide variety of GI symptoms as functional dyspepsia.

Fig. 2 Improvement in HADS scores by treatment



(Ko S et al. Digestive Medicine 2012; 55: 38-41)

Author Shigeru Ko, MD, PhD



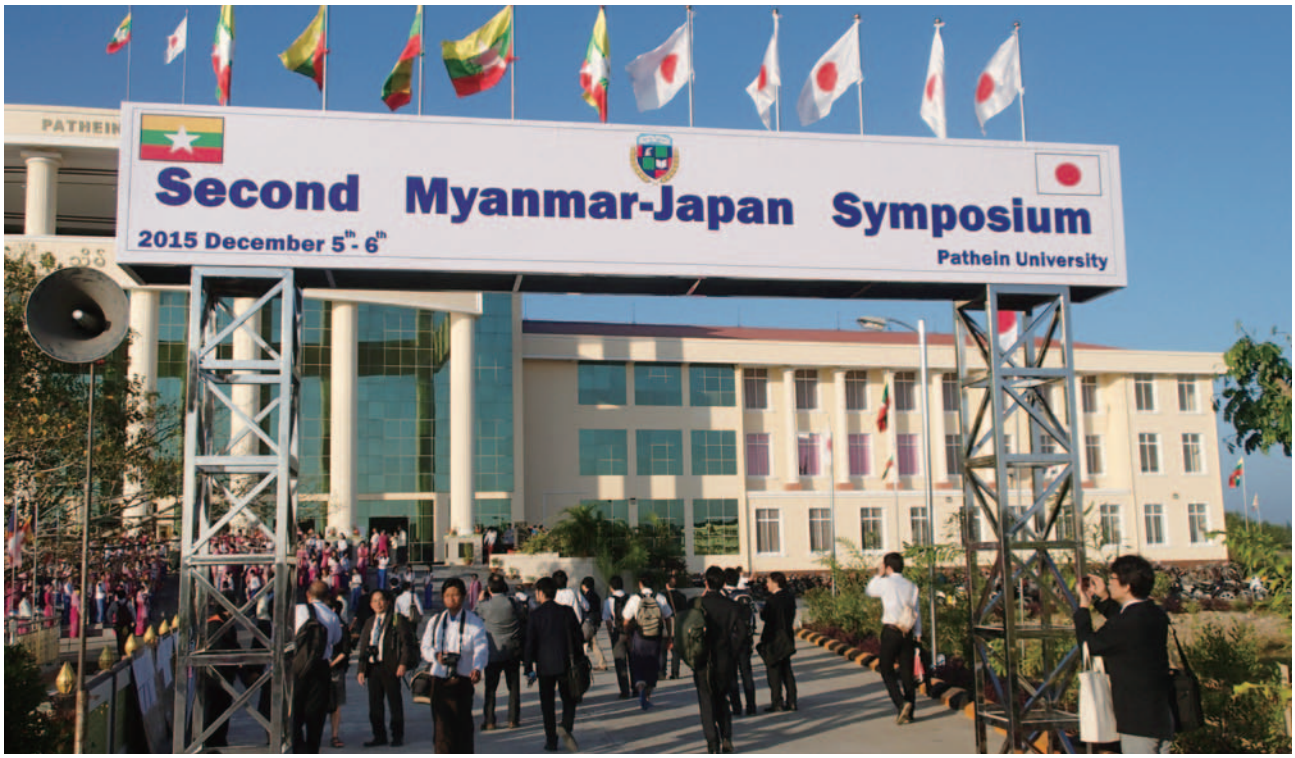
Associate Professor, Department of Systems Medicine, The Sakaguchi Laboratory
Keio University School of Medicine

【Background】

After graduating from Nagoya University School of Medicine in 1992, Dr. Ko was trained at Komaki City Hospital as general gastroenterologist. He completed his doctorate at Nagoya University Graduate School of Medicine in 1999. After receiving Ph.D degree, Dr. Ko spent two and half years at the University of Texas Southwestern Medical Center, department of Physiology as research fellow. After returning to Japan, he had been at Nagoya University School of Medicine, Department of Gastroenterology, and spent half a year at National Center for Geriatrics and Gerontology before he moved to Keio University. He is now an associate professor at the department of Systems Medicine, Keio University School of Medicine. He earned the Medical Research Encouragement Prize by the Japan Medical Association in 2010 for his research on molecular mechanisms of pancreatic regeneration. His specialties are pancreatology and regenerative medicine.

Report

Academic Exchange between Amano Enzyme and Asian Countries



Amano Enzyme has deepened its exchanges with Asian countries following on from its participation in a joint project with those countries, organized by the National Institute of Technology and Evaluation (NITE), a Japanese incorporated administrative agency. When the Convention on Biological Diversity (CBD) came into effect in 1993, it stipulated numerous conditions that had to be cleared in order to gain access to microbial genetic resources, including sharing profits with the resource country concerned. In line with these strict requirements, Amano Enzyme took part in a joint microbe research project set up by NITE to carry out microbial separation in Mongolia and Vietnam in 2012 and Myanmar in 2013, which led to the discovery of previously unknown useful enzymes. (Enzyme Wave, Issue 16)

Since then, we have built close ties with leading institutions in the field of microbial research in each of those three countries, and in 2014 and 2015 we participated in the First and Second Myanmar-Japan Symposiums hosted by Pathein University in the Republic of the Union of Myanmar as the only Japanese company to have announced applications for the global enzyme market and industry.

Nyunt Phay, president of the symposium's host Pathein University, is strongly promoting exchanges between Japan and Myanmar through education. Myanmar has achieved rapid economic development since introducing its democratization policy in 2011, and companies from other countries including Japan have been expanding their business in the country's future markets such as in infrastructure, the restaurant industry, retail, and new production bases. Amid this economic growth, we at Amano Enzyme are delighted to have contributed to Myanmar's development in the academic field, and intend to actively deepen this interaction in the future.

Conference presentation

In 2015 Amano Enzyme has decided academic presentations such as the following.
Please look forward to the activities of the future of Amano Enzyme.

Conference/Meeting	Date	Title	Speaker
1st International Symposium on Space Science of High Quality Protein Crystallization Technology	Mar. 5th, 2015 (Tokyo, Japan)	Development of Novel Enzyme Through High Quality Protein Crystallization Technology	Koikeda, S.
The 2015 Annual Meeting of Japan Society of Bioscience, Biotechnology and Agrochemistry	Mar. 29th, 2015 (Okayama, Japan)	'Tasty' health promoting method by oligosaccharide-producing enzyme(Luncheon seminar sponsored by Amano Enzyme)	Sasaki, M. Chaired by Shibata, K.
74th Annual SIT (Sugar Industry Technology) Technical Conference	May. 17th-20th, 2015(Osaka, Japan)	Dextranase and amylase for sugar production	Toyomasu, T.
The 46th Annual Meeting of Japan Pancreas Society	Jun. 19th, 2015 (Nagoya, Japan)	Comparisons of enzyme activities in various digestive enzyme preparations containing pancreatin.	Kuroda, M., Ko, S.
The 46th Annual Meeting of Japan Pancreas Society	Jun. 19th, 2015 (Nagoya, Japan)	Digestive Enzymes for Medicine – Visiting old, Learn new- (Luncheon seminar sponsored by Amano Enzyme)	Ko, S., Tando, Y., chaired by Nakamura, M.
9th Biotechnology Congress	Aug. 31th-Sep 2nd, 2015 (Orland, USA)	New concept of prebiotics: prebiotic enzyme Transglucosidase	Koikeda, S.
Enzyme Engineering XXIII	Sep. 6th-11th, 2015 (St. Petersburg, USA)	Protein engineering of alpha-glucosidase results in altered substrate specificity	Koikeda, S. Ishihara, S.
Enzyme Engineering XXIII	Sep. 6th-11th, 2015 (St. Petersburg, USA)	Development of oxidizing enzymes for hair dyeing	Hirose, Y.
The 15th Annual Meeting of the Food Enzyme Chemistry Society	Sep. 12th, 2015 (Tsu, Japan)	Characterization and application of a microbial β-amylase	Okada, M.
The 2015 Chubu and Kansai Branches Joint Annual Meeting of Japan Society of Bioscience, Biotechnology and Agrochemistry	Sep. 20th, 2015 (Toyama, Japan)	Comparative studies on the properties of digestive enzyme preparations for medicine.	Kuroda, M., Yamaguchi, S., Ko, S.
Japan Digestive Disease Week 2015(JDDW2015)	Oct. 8th, 2015 (Tokyo, Japan)	Comparisons of in vitro enzyme activities in complex digestive enzyme preparations prescribed in Japan.	Kuroda, M., Ko, S.
The 175th regular meeting of Chubu branch of the Japan Society for Bioscience, Biotechnology, and Agrochemistry, young member's symposium, "New carbohydrate materials and related enzymes"	Nov. 14th, 2015 (Tsu, Japan)	Current status of industrial carbohydrate-relating enzymes	Okada, M
The 61st Polarography and Electro-analytical Chemistry Panel Discussion	Nov. 24th, 2015 (Himeji, Japan)	Heparin determination by using enhance effect of enzyme reaction velocity by polylysine.	Uematsu, K., Ueno, T., Nishio, K., Suzumura, A., Yamaguchi, S., Katano, H.
The 46th General Meeting of The Japanese Society of Digestion and Absorption	Nov. 27th, 2015 (Chiba, Japan)	Comparisons of enzyme activities in various digestive enzyme preparations containing pancreatin.	Kuroda, M., Ko, S.
The Second Myanmar-Japan Symposium	Dec. 5th, 2015 (Pathein, Myanmar)	Industrial Applications of Enzymes	Yuki, K.

Journal and book

Journal/Book	Date	Title	Author
Technology and Market in Enzyme Applications 2015 (CMC Publishing)	May, 2015	Enzyme utilizations in pharmaceutical field (Chapter 10)	Kuroda, M.
FEBS Journal (Federation of European Biochemical Societies) 2015,282(13),p.2540	Jul, 2015	Crystal structure of β-galactosidase from Bacillus circulans ATCC 31382 (BgaD) and the construction of the thermophilic mutants.	Ishikawa, K., Kataoka, M., Yanamoto, T., Nakabayashi, M., Watanabe, M., Ishihara, S., Yamaguchi, S.
Nature Chemical Biology Vol.11 p.762-764	Aug, 2015	Monobody-mediated alteration of enzyme specificity	Tanaka, S., Takahashi, T., Koide, A., Ishihara, S., Koikeda, S., Koide, S.
Kagaku to Seibutsu (Japan Society of Bioscience, Biotechnology and Agrochemistry)2016, Vol.54, No.1 pp.61-64	Dec, 2015	Isolation of industrial enzyme-producing microorganisms.	Yamaguchi, S.

Symposium

Third Sino-Japan Joint Symposium on Enzyme Technology

The Third Sino-Japan Joint Symposium on Enzyme Technology was held on Saturday, October 31, 2015 at Jiangnan University in Wuxi, Jiangsu, China. Jointly held with Amano Enzyme and Jiangnan University, this symposium has been held every two years since 2011, with the aim of promoting the application research of enzymes in Asia through interpersonal relationship between Japanese and Chinese researchers who study enzymes. The symposium was well attended with a total of about 100 attendees from Chinese universities, enzyme related organizations, companies and so on.

Lecturers from both Japan and China gave talks on six themes. From Japan, Sakayu Shimizu (Professor, Faculty of Bioenvironmental Science, Kyoto Gakuen University and Professor Emeritus, Kyoto University) and Masaru Tanokura (Professor, Graduate School of Agricultural and Life Sciences, The University of Tokyo) were invited to speak. Below is a list of all the lecturers and the titles of their talks (in the order given).

①Song Kungang (Honorary Director the China Dairy Industry Association),
A new page in the China dairy industry

②Masaru Tanokura,
Structural basis and improvement of enzymes producing chiral compounds

③Sakayu Shimizu,
Thirty years of research and development in oleaginous microorganisms and future prospects

④Xinhui Xing (Professor, Department of Chemical Engineering, Tsinghua University),
Progress of Integrative Enzyme Engineering for Clean Heparin Pharmaceutical Industry

⑤Ruiting Guo (Professor, Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences),
The applications of X- ray protein crystal structure analysis on mechanism and modification of enzymes

⑥Jie Li (Professor, College of life Science, Northeast Agricultural University),
The development and expectation of expression system for Aspergillus niger

At panel discussion after the lectures the panelists Professor Shimizu, Professor Tanokura, Professor Guo and Professor Li, conveyed many messages to the young Chinese researchers attending such as their expectations for the future of enzyme research.

By continuing to hold this symposium in future, Amano Enzyme is committed to strengthening technology exchange between Japan and China and encouraging development of Sino-Japanese relations in the field of enzymes.

Information

Hello Tokyo from Japan

Introducing the Tokyo Office of Amano Enzyme Inc.

The windows on the 16th floor offer a wonderful view. The toing and froing of JR trains is fascinating for railway buffs, and the neon lights in the streets look pretty too. But this has not always been the location of our office.

Our former president and chairman, the late Motohiro Amano, started our sales operations from a single desk in Kanda in 1954 and established a sales office in Yaesu in 1964. The office later relocated to Shiba Park, where our current president Motoyuki Amano took up his position in sales. It was not until 1998 that we moved to our current location in the Imperial Tower.

While liaising closely with the Nagoya Head Office, we strive to expand our enzyme sales by building trust with our customers in the Kanto area and northward. Also, rather than make our very busy customers around Japan or abroad visit Nagoya for meetings, we often arrange meetings in the Tokyo office instead.

Yurakucho, Shinbashi, Ginza and Hibiya are our closest stations, and Hibiya Park is nearby too. Preparations are also underway for the 2020 Olympics. If you are visiting Tokyo and have some spare time, please do not hesitate to drop by our office. Of course we would be delighted to see you, even if it is just to share the view from our window.

Amano Enzyme Message Board (May - December 2016)

Exhibition Information

Please come to our booth!
We look forward to seeing all of you from around the world.

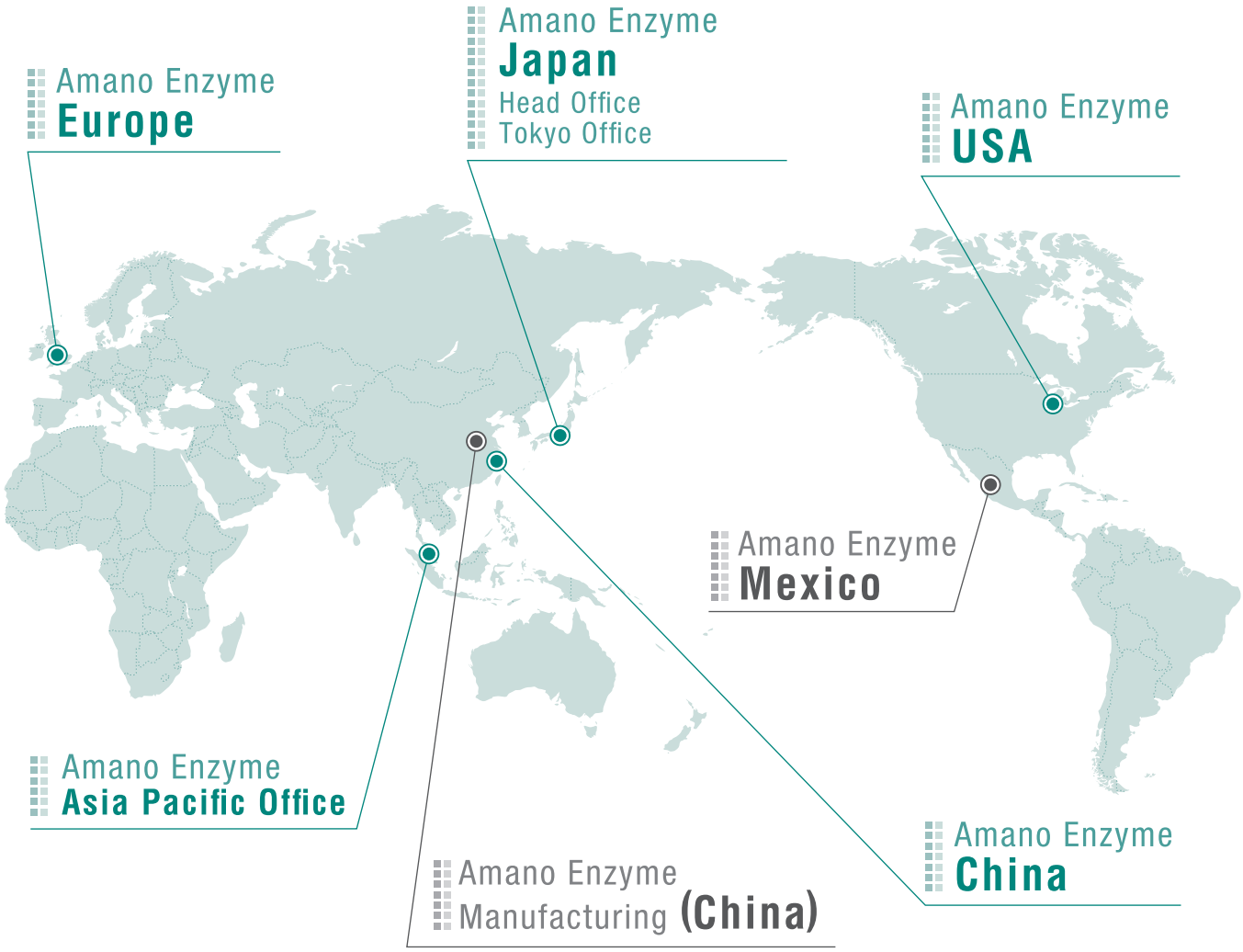
Date	Exhibition	Location
May 18～20, 2016	ifia Japan	Tokyo, Japan
June 21～23, 2016	CPhI China 2016	Shanghai, China
July 16～19, 2016	IFT 2016	Chicago, USA
September 21～23, 2016	Fi Asia 2016	Jakarta, Indonesia
September 21～22, 2016	Food Technology Summit&Expo 2016	Mexico City, Mexico
October 4～6, 2016	CPhI Worldwide 2016	Barcelona, Spain
October 4～8, 2016	Supply Side West	Las Vegas, USA
Nov29～Dec1, 2016	Hi Europe 2016	Frankfurt, Germany

Amano Enzyme participation status at 2015 exhibitions

During 2015, Amano Enzyme exhibited at various pharmaceutical and food industry-related trade shows at several locations around the world.
(Japan, China, Thailand, Spain, and the U.S.A.).

Amano Enzyme

World Network



◉Manufacturer

AMANO

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