Volume 22

Enzyme Wave

2019

AMANO
Amano Enzyme

MOON PARKA®

Kinetic Seat Concept

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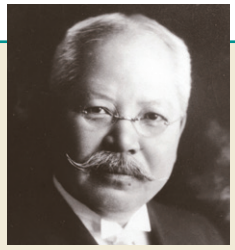
Jokichi Takamine Study Group, NPO

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)

Jokichi Takamine Study Group, NPO

The Jokichi Takamine Study Group, an NPO organization, has appointed Sakayu Shimizu as the new chairman from this year. The organization is planning to engage in even more activities, such as publication of its magazine and hosting lectures etc., so that many more people will learn about Dr. Takamine, a great advocate of the development of science and technologies and its industrialization in modern Japan. Furthermore, he had made substantial contributions to various activities, such as the establishment of the friendly relationship between Japan and the U.S.

Greeting from the new chairman

I first read about Dr. Jokichi Takamine from a picture book published by Kodansha when I was a child. About ten years ago when I attended a lecture of Mr. Yutaka Yamamoto, the honorary chairman of this Study Group, I learned for the first time about Dr. Takamine's great achievements. I had learned that during the chaotic period toward the end of the Edo era when Ryoma Sakamoto and Takamori Saigo were playing crucial roles in the society, the young Dr. Takamine, who was with high expectations from the feudal domain, had studied among adults at the age equivalent to a junior high school student nowadays. I had also learned that Dr. Takamine had subsequently made great contributions in various fields, including biotechnology, politics, economy, and the Japan-U.S. relationship, both in Japan and the U.S. I was simply surprised and impressed by his ability as a human being, which was beyond the boundaries of national powers and cultural differences. I think the word "pioneer" is the best word to describe him. This year, I am honored to be appointed as the chairman of this Study Group after Mr. Yutaka Yamamoto, the honorary chairman, and Mr. Mitsuo Ishida, the former chairman. I am quite nervous about whether I can fulfill the role as the chairman because it has been done so splendidly by my predecessors who are the experts in the study of Dr. Takamine. I sincerely appreciate your support. (Sakayu Shimizu)

July 22, 2018, Chairman Shimizu visiting Aoyama Cemetery on the anniversary of the death of Jokichi Takamine

March 2018, "The pioneer of chemical entrepreneurs, References of Jokichi Takamine" was certified as Chemical Heritage #46.

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.

The Secretariat

The Prof. Jokichi Takamine Research Foundation
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*For further details, visit our website : http://www.npo-takamine.org/ask.html

Trend

SDGs is the chance of growth for Japan

Introduction of the author

Norichika Kanie

Professor at Graduate School of Media and Governance, Keio University
Senior Research Fellow at the Institute for the Advanced Study of Sustainability, United Nations University (UNU-IAS)

[Background]
Appointed to the current position in 2015 after working as a lecturer and assistant professor at the University of Kitakyushu and associate professor at the Graduate School of the Tokyo Institute of Technology
Held positions as Marie Curie International Incoming Fellow at the European Commission and visiting professor at Sciences Po., Paris.
Specialty is in international relations study and global system governance
The authority of SDGs study who successfully engages in both researches and practical works

The interest in SDGs is rapidly increasing. Although only less than 20% of the general public is interested in it at this point, I feel that companies and governments have become increasingly more interested in this field over the past year or so. According to the survey that the Government Pension Investment Fund (GPIF) conducted last year targeting 2052 companies listed on the First Section of the Tokyo Stock Exchange, more than 60% of the companies responded that they had started actions or were planning to take some kind of actions in regard to SDGs. I imagine that more companies are on the same track today. When I am walking in Otemachi, Tokyo, I notice many people wearing SDG badges, which is probably thanks to the encouragement by the Keidanren. The badge is the same one as the colorful badge that Mr. Nakanishi, the chairman of Keidanren, is often seen wearing during a press conference.

Around 2015 and 2016 when SDGs were introduced to the world, the department assigned to corporate social responsibility (CSR) in companies first started paying attention to SDGs. The 17 goals and 169 targets provided in SDGs were received as a great tool for companies to display their CSR and social contributions. As time goes by, however, owners of companies gradually started to become interested in SDGs.

Why is that?

Most of the management principles and corporate principles that founders of companies advocated mentioned their will to do good for society and make society better. The idea of companies is as follows. Entrepreneurs found companies to improve society, but the reality is far from ideal. Therefore, they come to a conclusion that the reason for the existence of their companies is to fill in the gap. The reason that business owners with foresight take the initiative in proceeding with SDGs activities in their main operations is that their principles and SDGs are facing the same direction.

All the member states of the United States support SDGs. The United States under the leadership of the Trump administration and North Korea are not exceptions. This means that SDGs is the ideal form of the future that all the nations envision. By translating corporate principles into the form of the future expressed in a universal language, it can more easily express the contribution toward universal values, so to speak. Then, if they can conduct businesses by grasping the values ahead of others, they can make great revenues. Realizing SDGs is now a natural process for business owners.

I feel there are mainly two essential points to keep in mind when one is seriously incorporating the form of the future into a business. One is to turn away from the future and solve current

problems. I have an experience of clarifying hidden problems by making an ideal form as a starting point. A method like this is called back casting. Another point is to think using 17 viewpoints. It means the use of the 17 goals of SDGs. To start, you can select one of the goals. Still, you can move closer to the ideal future as you review problems from 17 viewpoints and resolving one problem at a time.

An example is the food. You probably come up with food production to overcome issues such as nutrition and health (goal 3). Yet, you should not stop making progress there. You may be able to reduce food waste by half by 2030 (target 12.3). You may be also able to change food package to no-plastic materials (goal 12). It is also possible to improve efficiency by switching energy sources for production processes to renewable energies (goal 7). The improvement of efficiency also leads to the increase of profit (goal 8).

It is important to set a grand goal to motivate and use internal resources of a company to take actions and to improve corporate image. By setting a grand goal, awareness and resources become shifted toward it even though there is no guarantee that the goal can be achieved in 2030. The aim of SDGs is there.

Various ideas come in handy when taking such actions. When proceeding with flexibility and tolerance to take in diversified ideas, it would motivate employees as well (goal 8). Serious efforts will surely encourage increasing investments in sustainability.

SDGs are a great opportunity for Japan where the population is decreasing, and the establishment of a new business model is in dire need. The U.N. Summit with the theme of SDGs will be held in 2019. We wish to transmit new models from Japan to the world and seize opportunities.

Column

Protein as a next-generation industrial material

Introduction of the author

Junichi Sugahara

Sugahara co-founded Spiber in 2007. He engaged in the development of low-cost production technologies of structural protein and processing technologies for it as a R&D executive. He obtained a PhD at Keio University specializing in bioinformatics.

Attractiveness of protein material

The strength per weight of a spider silk that a spider uses as a lifeline is 340 times higher than iron. It exhibits an extremely high shock absorption property. The teeth of the ant is as hard as a titanium alloy. The amazing ability of the grasshopper and flea to jump is enabled by the high-performance rubber tissues in their legs. Wool and cashmere are familiar materials originating in organisms. The heat retaining ability and texture have excellent characteristics as the material of clothes. Protein is the main component of all of these materials.

The spread of protein materials that do not depend on petroleum as the raw material is important in realizing a sustainable society that is founded on the circulation of materials available on land. Yet, there are many hurdles to overcome before realizing this goal. Raising sheep and goats requires a great deal of labor, water, and land. It is also difficult to quickly increase their supplies. Many animals, like spiders, are not suited for domestication. Production using genetically modified microorganisms is not easy, either. Although many researchers have attempted it in the 1990s, protein that was used as the material had the tendency to become highly polymerized and highly repeated, and the production of microorganisms was extremely difficult.

Activities of Spiber

Under such circumstances, biotechnology entered a new phase in the 2000s. Whole genome sequencing, the design of an organism, was conducted one after another, and IT technologies to analyze genome sequencing also became common. Spiber that was founded in September

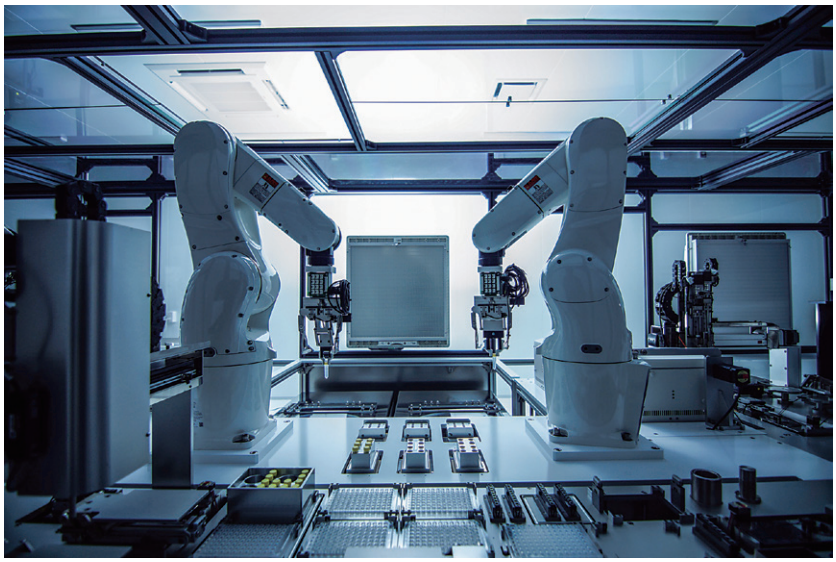


Figure 1. Experiment automation system in development

2007 also started by extracting the characteristics of gene sequences that were likely to be expressed in the host organisms by analyzing massive amounts of life information and reflecting the information on the genes of spider silk. To explore molecular design that perform well under all conditions, including culturing, refining, and material processing, Spiber automated experiments and created database (Figure 1) and screened more than 1,200 types of molecular designs and optimal production conditions. As a result, Spiber discovered a possibility of reducing the production cost of protein material, including spider silk to a level that was feasible as an industrial material.

In 2013, we started the operation of a pilot plant of fermentation and spinning jointly with Kojima Industries, an automotive component manufacturer. We promoted product development using materials produced at the plant while conducting experiments on production technologies. In 2015, with The North Face we announced Moon Parka®, the world's first clothing made with artificial spider silk produced using an actual production line. In 2016, our artificial spider silk was used in the Kinetic Seat Concept, the next-generation car seat announced from Toyota. We believe that we were able to present a future where protein would replace petroleum materials through these concept products (Figure 2).

MOON PARKA®　　Kinetic Seat Concept

Figure 2. Samples of products produced using protein materials we produced

For further acceleration

There are many more things to do to reduce the cost and increase the function of protein materials. The use of enzymes is one of them. The development of optimal enzymes may realize a great cost performance that would lead the world in processes and materials, such as the improvement of the collection rate during production and the improvement of materials. We are going to keep working on the production of the best things with companies with excellent technologies.

Report

Exploration of Microorganisms in Collaboration with Japan Monkey Centre

The exploration of new microorganisms is essential for the development of new enzymes. Amano Enzyme has been continuing its own explorations of microorganisms, as well as joint explorations with top-level research facilities. As one of the examples of such explorations, today we are going to introduce our collaborative research with the Japan Monkey Centre.

The Japan Monkey Centre in Inuyama City, Aichi, Japan, is the world's largest primate zoo that keeps about 900 monkeys (primates) in 60 species. It is in a cooperative relationship with the Primate Research Institute, Kyoto University, which is one of the top-level research facilities in the world. Although it is a zoo, the latest primate research is conducted there. It is also frequently hosting study sessions to learn about primates targeting children as open events.

Amano Enzyme has been conducting collaborative research with the Japan Monkey Centre since 2016. We are exploring the possibility of isolating intestinal bacteria from primates at the Japan Monkey Centre and use them as the source of new enzymes. Through this collaborative research, we are finding bacteria considered new species.

All individuals of the primates kept at the Japan Monkey Centre are the subject of collaborative research. Yet, we first focused on the feeding habits of individual species and started our research by prioritizing ones known to have distinctive feeding habits. While many primates mainly feed on fruits, we focused on the *Colobus* that mainly feeds on tree leaves. While the *Colobus* is a primate, it has multiple stomachs like the cow and is characterized by the ability to digest fibrous leaves. We expect to find intestinal bacteria with enzymes that can efficiently digest dietary fiber. For the above reasons, we started our research using the *Colobus* as the first subject.

We collected samples from the *Colobus* that we used as the subject. We then cultured the samples under special conditions where intestinal bacteria such as lactic acid bacteria and individually isolated them.

We analyzed the genes of the isolated microorganisms and determined their species names. Among the 114 strains that we isolated, 7 strains and 4 species were assumed to be new species that were discovered for the first time.

We presented these findings in the 62nd Primates Conference held at the Japan Monkey Centre in January 2018. This is where outcomes of the latest primate researches are reported.

Our later research successfully isolated intestinal bacteria that was even more difficult to isolate as they can't survive in aerobic condition. We are going to continue our joint research with the Japan Monkey Centre to further explore effective enzymes in the intestinal bacteria of the primates.

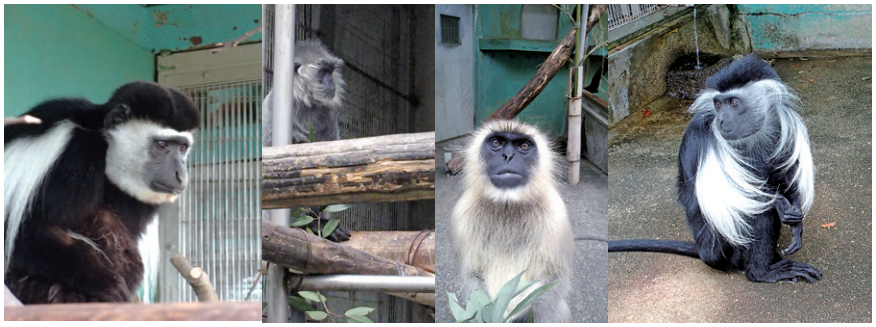


Figure 1. Individuals of the *Colobus* we are studying

Figure 2. Isolation of intestinal bacteria

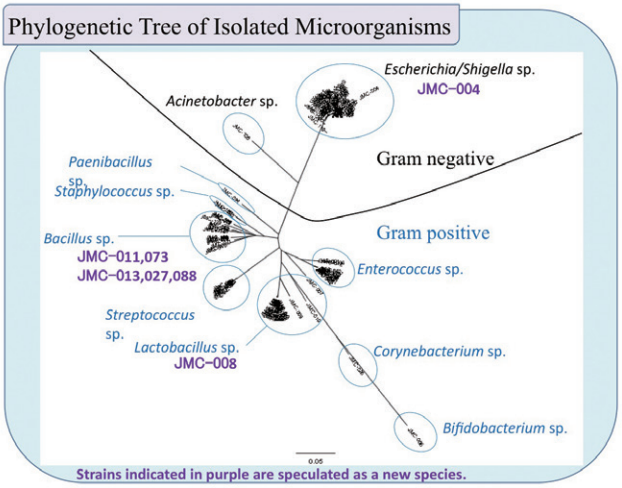


Figure 3. Model showing the diversity of intestinal bacteria (phylogenetic tree)

Introduction of the author

Kensuke Yuki

R & D Support Division, Gifu R & D Center, Marketing Headquarters

[Background]
1994: Employed by Amano Pharmaceuticals (current Amano Enzyme)

Product introduction

Chiral Enzyme Spectrum "Amano"

Chiral Enzyme Spectrum "Amano" is an enzyme screening kit for the synthesis of chiral compounds. Amano Enzyme is offering it free of charge. This kit has been used by many customers for numerous screenings, and would be a useful addition to have on hand at your labs.

The kit contains several kinds of enzymes useful for chiral compounds production, such as Lipases, Esterases and Ketoreductases. Additional enzymes which are currently under development will be added from time to time. Amano is also pleased to work together with your lab to further improve our enzyme properties.

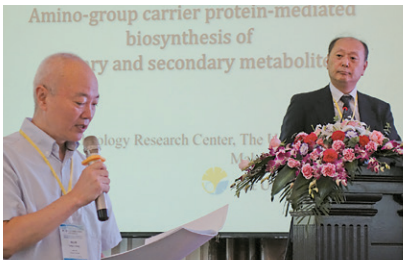
Symposium

The 2nd Sino-Japan Symposium on Biocatalysis and Biotransformation

The global environmental regulations are becoming stricter than ever. Especially in Asian countries, including China, environmental pollution associated with rapid development in the chemical industry has been a social problem. Some countries and regions are enforcing strict measures, such as the shutdown of factories. Under such circumstances, the importance of industrial processes that minimize harmful effects on humans, ecosystem, and the environment is increasing. The use of enzymes is a sustainable method that contributes to the foundation of green chemistry, because enzymes can produce chemical products under environmentally friendly conditions.

On August 25, 2018, Amano Enzyme held the 2nd Sino-Japan Symposium on Biocatalysis and Biotransformation at Hangzhou, China, jointly with Hangzhou University, following the first symposium in 2016. This symposium was held under the initiative of Professor Yang Li-rong at Hangzhou University, to connect Chinese companies interested in green chemistry that used enzymes and universities or public research facilities engaged in the latest research in this field. About 180 participants from Chinese companies and universities attended this symposium, and lectures in the following 13 titles (table below) were given, including lectures by Prof. Makoto Nishiyama (The University of Tokyo) and Prof. Jun Ogawa (Kyoto University), who were invited from Japan. Participants engaged in lively Q&As and discussions and made this symposium a huge success.

The attention toward enzymes in China has been increasing as indicated by the number of participants that had doubled from the first symposium. Amano Enzyme plans to continue organizing this symposium to help people with green chemistry using enzymes.



Prof. Yang Lirong (Zhejiang University)

Prof. Makoto Nishiyama (The University of Tokyo)

Prof. Jun Ogawa (Kyoto University)

Dr. Shotaro Yamaguchi (Amano Enzyme Inc.)

Makoto Nishiyama	The University of Tokyo	Amino-group carrier protein-mediated biosynthesis of the primary and secondary metabolites
Yang Sheng	Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences	Preparation and application of enzymes produced by Escherichia coli
Rao Zhiming	Jiangnan University	Construction of Corynebacterium sp. cell factory for efficient synthesis of highvalue amino acids and the industrial application
Jun Ogawa	Kyoto University	Microbial metabolisms pioneering novel enzymatic and microbial bioprocesses
Yuzo Kojima	Amano Enzyme Inc	Amano's Biotransformation Enzymes for Chiral Synthesis
Zhou Jiahai	Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences	Structural, mechanism and dynamics of complex enzymes
Wu Bian	Institute of Microbiology, Chinese Academy of Sciences	Computer design of enzymes: from concept to industrial application
Lou Wenyong	South China University of Technology	Biocatalysis technology and its application
Zheng Renchao	Zhejiang University of Technology	Development and application of nitrile-converting enzymes as biocatalysts
Hu Qiannan	Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences	Data-driven rational cell factory design using comprehensive enzymatic reactions
You Chun	Tianjin Institute of Biotechnology, Chinese Academy of Sciences	The construction of in vitro synthetic biosystems using oligosaccharides as starting materials based on phosphorylase
Li Aitao	Hubei University	Important biocatalytic element: Cytochrome P450 monooxygenase
Wu Mianbin & Yang Lirong	Zhejiang University	Improving the substrate selectivity of xylose reductase simultaneously using molecular mutation and metabolic pathway modification

Conference presentation

In 2018 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
DDW 2018 (Digestive Disease Week)	June 3rd, 2018 (Washington DC, Japan)	MIXTURE OF GLUTEN-DIGESTING ENZYMES IMPROVED THE SYMPTOMS OF NON-CELIAC GLUTEN SENSITIVITY:A RANDOMIZED SINGLE-BLIND, PLACEBO-CONTROLLED CROSSOVER STUDY	Sasaki, M., Takahashi, A., etc.
58th Japan Starch Round Table	June 8th, 2018 (Shizuoka, Japan)	Monobody -mediated alteration of enzyme specificity	Tetsuya Takahashi
49th Annual Meeting of Japan Pancreas Society	July 30th, 2018 (Wakayama, Japan)	Comparison of digestive activity of digestive enzyme formulas with the digestive tract model(2nd report)	Takahashi, A., Kuroda, M., Ko, S.
9th International Congress on Biocatalysis	Aug. 29th, 2018 (Hamburg, Germany)	Amano' s biotransformarion enzymes for chiral synthesis	Sato, Y.
26th Young Pancreas Research Conference	October 31th, 2018 (Kobe, Japan)	Comparison of digestive activity of digestive enzyme formulas with the digestive tract model	Takahashi, A., Ko, S.
		Comparison of digestive activity of digestive enzyme formulas with the digestive tract model simulating low intestinal pH	Ko, S., Takahashi, A.
49th Annual Meeting of Japan Digestive and Absorption Society	Nov. 17th, 2018 (Chiba, Japan)	Comparison of digestive activity of digestive enzyme formulas with the digestive tract model (Panel discussion)	Takahashi, A., Ko, S.
		Comparison of digestive activity of digestive enzyme formulas with the digestive tract model(Poster session)	Ko, S., Takahashi, A.
16th Annual Meeting of International Federation for Adipose Therapeutics and Science (IFATS2018)	Dec. 15th, 2018 (Las Vegas, USA)	Effective collection of stromal vascular fraction (SVF) by enzymatic treatment	J, Escalante., Mori, M.

Journal/Book	Date	Title	Author
Clinical and Translational Gastroenterology 2018 Sep 19;9(9):181.	Sep, 2018	Combination of Gluten-Digesting Enzymes Improved Symptoms of Non-Celiac Gluten Sensitivity: A Randomized Single-blind, Placebo-controlled Crossover Study	Ido, H., Sasaki, M., et al.
Saiseiiryou 2018, Vol 17, p.434-436	Nov, 2018	Amano Enzyme Inc. -Enzymes support the regenerative medicine-	Furukawa, K.

2019 Exhibitions

Date	Exhibition	Location
April 30 - May 2	CPhI North America 2019	Chicago(USA)
May 7-9	Vitafoods Europe 2019	Geneva(Switzerland)
May 21-22	2019 Protein Trends & Technologies Seminar	Itasca(USA)
May 22-24	ifia Japan 2019	Tokyo(Japan)
May 29-31	12th Protein Summit 2019 North-America	Saskatoon(Canada)
June 2-5	IFT 19	New Orleans(USA)
June 18-20	CPhI China 2019	Shanghai(Chaina)
July 7-11	BioTrans 2019	Groningen(Netherlands)
August 4-8	71st AACC Annual Scientific Meeting & Clinical Lab Expo	Anaheim(USA)
September 11-13	Food Ingredients Asia 2019	Bangkok(Thailand)
September 15-19	Enzyme Engineering XXV	Whistler(Canada)
September 25-26	Vitafoods Asia 2019	Singapore
October 2-4	14th Protein Summit 2019	Lille (France)
November 26-28	CPhI India 2019	Delhi(India)
December 3-5	Food Ingredients Europe	Paris(France)
December 4-7	IFATS	Marseille(France)

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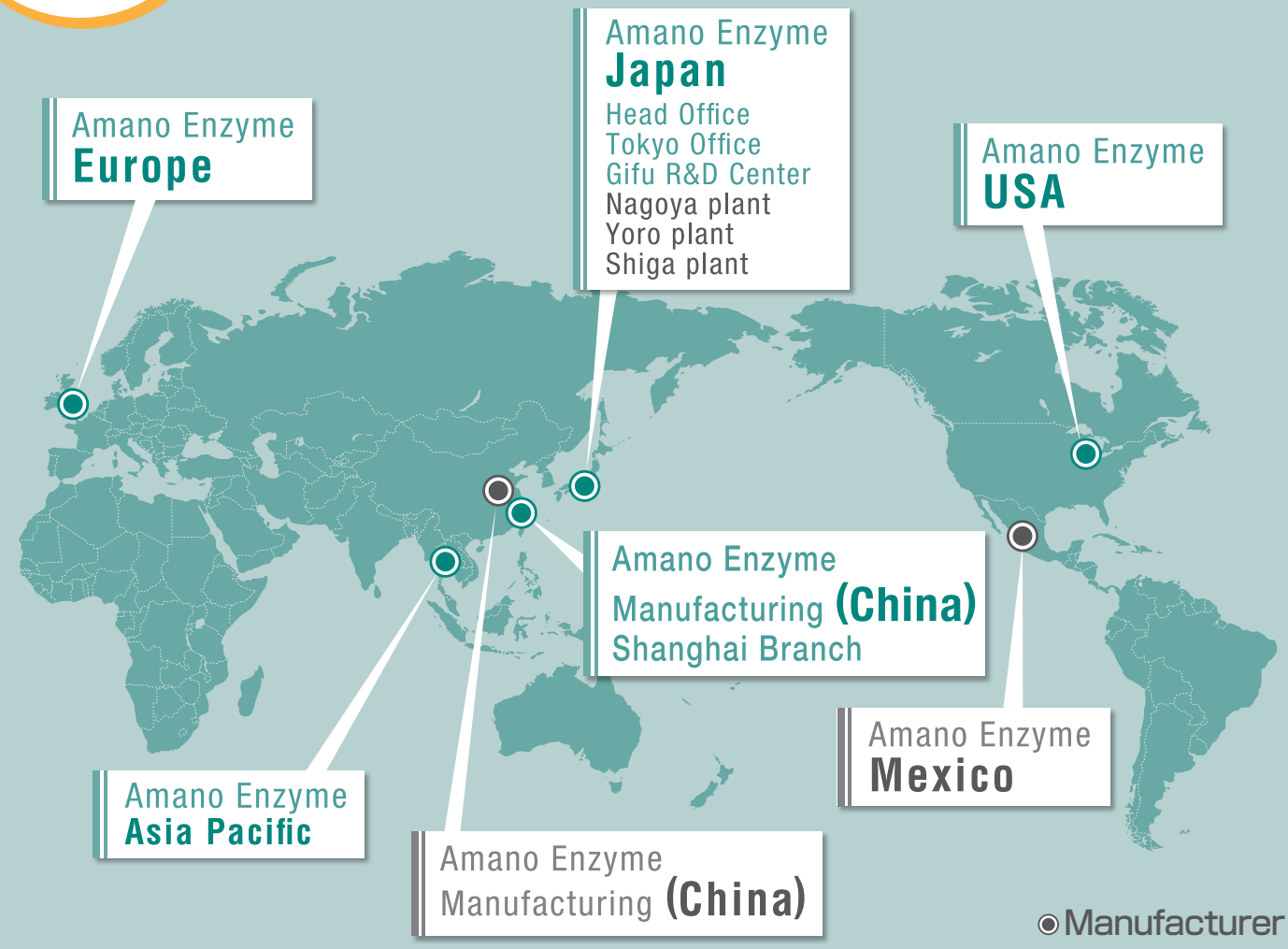
World Network



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