AminoScience and the Pursuit of New Possibilities

The Ajinomoto Group has continued to develop new amino acid technologies, placing them at the foundation of R&D efforts. Today, the Group prides itself on being a driving force in global amino acids research. It is said that the stirrings of life began more than three billion years ago with the creation of amino acids and other substances that would later form the bodies of organisms in primordial oceans (The Origin of Life, by Alexander Oparin). In other words, to study amino acids is to unravel the secrets of all life on earth. The Ajinomoto Group calls this pursuit of harnessing the potential of amino acids “AminoScience.” Comprising a pillar of its business alongside consumer foods, the AminoScience segment comprises two parts: Life Support (animal and plant nutrition, highly functional materials) and Healthcare (pharmaceuticals, advanced medical treatment, health and nutrition). By advancing research in these domains, the Group aims to improve nutrition for all living things.

Amino acids are said to have various functions that have yet to be elucidated. To bring their mechanisms to light and mobilize them for the well-being and sustainability of humans and all other life on earth, the Group will continue to advance R&D and its business.

Improving the Nutrition of All Forms of Life with World-Leading Amino Acid Technologies

Amino acids are not only the building blocks of all life on earth; they are also substances with a myriad of undiscovered possibilities. Since its founding, the Ajinomoto Group has studied amino acids with the goal of harnessing their various functions in products. Putting its world-class AminoScience expertise to use for better nutrition and health is just another example of how the Group is capitalizing on its unique business specialties.

R&D that drives innovation

R&D at the Ajinomoto Group is aimed at leveraging its unique AminoScience expertise for proposing new value-added materials and business models that propel growth. The Group has dozens of research laboratories across 14 countries worldwide, employing more than 1,700 R&D employees. These resources make it possible to propose custom solutions to global markets through interdisciplinary partnerships. The number of patents held by the Ajinomoto Group totaled 864 in Japan and 3,348 in all other countries as of March 2015. The Group is also focused on creating value through open and linked innovation, where outside ideas and technologies are incorporated into development with other entities.
Understanding Amino Acids and Their Benefits

All proteins consist of just 20 kinds of amino acids

Approximately 20% of the human body is made up of proteins. Proteins not only form the physical structure of muscle, skin, hair, and other tissue, but also serve a role in immunity as enzymes, hormones, and antibodies. They can also be nutrients or parts of blood. Proteins thus coordinate and control various reactions in the human body.

These proteins are made up of 20 kinds of amino acids—the same 20 amino acids that make up the proteins of all living things on earth, not just humans. These amino acids come in two basic varieties: essential amino acids, which can’t be synthesized within the body and therefore must be obtained from food, and non-essential amino acids, which are synthesized within the body on a regular basis. Because the amino acids that make up proteins serve a crucial function in sustaining the life of animals, it is important to get all of them as part of a balanced diet.

The multifaceted roles of amino acids in the body

Amino acids are not only the building blocks of proteins. Individual amino acids play a variety of roles, involved even in taste. The meat, fish, vegetables, fruit, dairy products, fermented foods, and seasonings we eat everyday, for example, contain various amino acids that are a defining part of how the food tastes. Of those, the greatest contributor to umami is glutamic acid. Glutamic acid is one of the most commonly occurring amino acids in the natural world, and all organisms make glutamic acid in their bodies. It not only makes food more delicious, but also performs various functions essential to survival. Even breast milk, a newborn’s first food, is rich in glutamic acid. The glutamic acid that creates the experience of umami in food and the glutamic acid produced in our bodies are the same substance. Research on its various functions is being pursued in Japan and other countries worldwide, shedding scientific light on its contributions to health.
The flavor and health benefits of umami and kokumi substances

While studying these various functions of amino acids, the Ajinomoto Group has also been developing technologies that enhance the experience of eating in general, including taste, texture, and flavor. The Group also strives to utilize the flavoring compounds and seasonings resulting from these technologies for improving health.

One such effort is reducing salt intake. The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) are both working to reduce salt intake, while hampered by the fact that reduced-salt diets taste less flavorful and satisfying. Meanwhile, the National Academy of Sciences reports that targeted use of umami compounds can help reduce salt content while maintaining flavor. The Ajinomoto Group thus has sought to contribute to salt reduction using its extensive knowledge of umami. YASASHI®², which provides the same salt flavor with 50% less sodium, is one outcome of this endeavor.

Another area of focus is “kokumi” substance, which enhances the five basic tastes (sweet, sour, salty, bitter, and umami), deepening and rounding out their flavor and improving palatability. In August 2014, the kokumi substance glutamyl-valyl-glycine¹, for which Ajinomoto Co., Inc. has developed a production method, was approved as a food additive by Japan’s Health Ministry. Kokumi ingredients have already been introduced in products overseas, while in Japan their introduction has started with certain household dashi products in fiscal 2015.

Confirmed safety of monosodium glutamate

Monosodium glutamate (MSG) has passed all of the numerous safety tests that are required for a food additive used as seasoning under Japan’s Food Sanitation Act.

In 1987 the Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated MSG’s safety based on test results from research institutions worldwide and concluded that, because MSG poses no harm to human health, its acceptable daily intake need not be specified. In 1991 the European Community’s Scientific Committee on Food (SCF) reached the same conclusion, and in 1995 the U.S. Food and Drug Administration (FDA), based on an evaluation report it commissioned from the Federation of American Societies for Experimental Biology (FASEB), reiterated MSG’s safety. Again, in 2003, Food Standards Australia New Zealand (FSANZ) released a safety evaluation report with the same findings.

The Ajinomoto Group believes umami compounds still have much to offer, for making daily foods more delicious, and for maintaining human health. By continuing to search for those benefits, the Group hopes to contribute to the health of people all around the world.

¹ A tripeptide (class of molecules comprising a chain of three amino acids linked in a specific order) consisting of glutamic acid, valine, and glycine. Present in foods that are already consumed, such as scallops, naturally brewed soy sauce, and fish sauce, it enhances kokumi.

² A service that supplies oligonucleotide and peptide drug substances using a unique liquid phase synthesis. It employs the world’s first practical liquid phase method to synthesize oligonucleotides at the kilogram scale. The technology is a very powerful tool for the predicted large-scale need of oligonucleotides.

³ A service that supplies proteins using a unique technology that harnesses the abilities of amino acid-producing bacteria. The numerous advantages make it possible to produce various proteins that are difficult to produce with conventional technologies.

The Ajinomoto Group has been developing unique hybrid processes combining fermentation and chemical synthesis technologies and applying them to the development of pharmaceutical intermediates derived from amino and nucleic acids. These activities evolved into a bulk pharmaceutical intermediate supply business, later expanding into our very-own, unique biopharmaceutical manufacturing technologies and business.

The Ajinomoto Group now provides the Ajiphase®² service business for contract manufacturing of oligonucleotides and peptides, and Corynex®³ for contract development and manufacturing of proteins.

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Highlight Developing biopharmaceutical technologies

Technology evolution from amino acids to peptides to proteins

Amino acids Dipeptides Peptides Proteins

Small molecules Large molecules

Fermentation Enzymes Synthesis Fermentation

MSG Aspartame Recent R&D

Feed and pharmaceutical-use amino acids

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Amino Acids for Medicine and Health

Our journey from amino acid supplier to drug designer

Hydrolysis of wheat gluten or soy protein produces a liquid containing amino acids. Of these, Ajinomoto Co., Inc. had only extracted glutamate at first. Along the way, however, the company saw the potential to isolate and extract the remaining amino acids, for use in the pharmaceutical field.

This led to the development of technology for isolating and refining amino acids, and the company had successfully isolated 18 amino acids by the beginning of the 1950s. These were delivered to researchers in Japan and worldwide, providing the impetus for global research into the uses of amino acids. As of 2014, the global demand for amino acids for pharmaceutical use is estimated at around 30,000 tonnes—and Ajinomoto Co., Inc. is the leading company in this field.

Ajinomoto Pharmaceuticals Co., Ltd. is tasked with applying its extensive amino acid knowledge and advanced technologies to new drug development. Specializing in gastrointestinal disorders, the company strives to develop drugs that regulate food and nutrient digestion, absorption, metabolism, and excretion.

LIVACT® Granules, a branched-chain amino acid formula marketed since 1996, improves the nutritional condition of decompensated cirrhosis patients. The drug was released in the Philippines in January 2015 and in Vietnam in August 2015. Given dietary culture and body-type similarities between Japan and Southeast Asian countries, the company sees potential for business expansion by extrapolating the results of Japanese clinical studies. With LIVACT® Granules, Ajinomoto Pharmaceuticals Co., Ltd. wants to help improve the quality of life (QOL) of cirrhosis patients all across Asia.

“AminoIndex Technology” contributes to cancer and metabolic disease prevention

It is now understood that when a person becomes sick, their metabolic balance often changes, altering the concentration of amino acids in their blood. Ajinomoto Co., Inc. utilized this observation to develop AminoIndex™, an “AminoIndex Technology” that measures blood amino acid concentrations to detect disease risk. One advantage it provides is the ability to quickly determine a patient’s health condition using a small blood sample.

AminoIndex™ Cancer Screening (AICS), a service jointly launched with SRL, Inc., assesses risk of multiple types of cancer by analyzing blood amino acid concentrations. In August 2015, a screening test that provides early detection of pancreatic cancer was added to AICS. Around 60% of pancreatic cancer cases are said to be inoperable at diagnosis, with a five-year survival rate of only 7%. Early discovery with AICS thus holds promise for prolonging life and increasing chances of remission.

The Ajinomoto Group is also endeavoring to use “AminoIndex Technology” for preventing diseases other than cancer. AminoIndex™, Metabolic Screening (AIMS) is a test that assesses multiple risks arising from nutritional status and lifestyle. Because amino acid concentrations shift in cases of visceral fat accumulation, fatty liver, and postprandial hyperglycemia, AIMS is intended to help with preventing the serious onset of disease by assessing the risk of these conditions so they can be addressed early on.

The Ajinomoto Group will continue to utilize “AminoIndex Technology” for helping people live longer, healthier lives.
Developing a safer iPS cell culture medium

Since 1987 Ajinomoto Co., Inc. has been using its knowledge from decades of amino acids research to market culture media used in the production of biopharmaceutical products.

In February 2014 the company, working with the Center for iPS Cell Research and Application at Kyoto University, succeeded in developing StemFit® AK03, a safer iPS/ES cell culture medium for regenerative medicine applications.

Typically human iPS cells are cultured with mouse cells called “feeder cells,” using a culture medium that includes bovine serum. StemFit® AK03 uses recombinant proteins, a type of bioengineered protein, thereby eliminating animal- and human-derived components and creating a medium consisting solely of highly refined substances.

A consultation on the safety and quality of StemFit® AK03 cell culture medium with Japan’s Pharmaceuticals and Medical Devices Agency (PMDA) confirmed that the product does not include any raw materials subject to the Standards for Biological Ingredients. Ajinomoto Co., Inc. believes this confirmation to be important from a safety viewpoint.

Supporting athletes with Ajinomoto’s original amino acid formulations

Taking adequate amounts of amino acids, the building blocks of proteins, is essential for athletes and sports enthusiasts who train hard. Amino acids are convenient because they can be taken when needed, being absorbed by the body in only around 30 minutes, and are safe substances not prohibited by anti-doping regulations.

Ajinomoto Co., Inc. has been conducting scientific research on sports and nutrition with the goal of supporting top athletes.

One product of this research is amino VITAL® GOLD, which features an amino acids mixture enriched with leucine as its main ingredient. This product was engineered to address the problem faced by the world’s leading competitors where lingering fatigue from strenuous daily practice or training impedes continued exercise. It is used fondly by current and aspiring top athletes alike.

amino VITAL® Amino Protein, with a mixture of essential amino acids and whey protein, provides the same body-building support as ordinary protein products but at a smaller serving size (approximately 4 grams compared to the usual 20 grams).

And amino VITAL® Perfect Energy, an alanine and proline-enriched formulation combined with carbohydrates, helps athletes who take it during prolonged practice or a game to perform at their peak to the very last round or inning.

Highlight

Promoting deeper, more restful sleep: Glyna® remarked as food product with functional claims

Glycine, an amino acid, is found in high amounts in scallops and other seafood, and also constitutes one third of the collagen in human skin.

Through many years of amino acids research, Ajinomoto Co., Inc. discovered that taking glycine quickly works to induce deep sleep (slow-wave sleep), and acquired a patent in Japan (No. 4913410). In 2005, it released Glyna® in Japan, a sleep aid containing 3,000 milligrams of glycine now used by more than a million people.

To more clearly and appropriately display the product’s functional information as backed by scientific evidence, in August 2015 the company re-released Glyna® as a food product with functional claims under new guidelines of the Consumer Affairs Agency in Japan.

Notification for food with functional claims

This product contains glycine, a substance that has been shown to rapidly induce deep sleep and enhance sleep quality (improved sleep rhythm and perception of sleep depth), while also contributing to a more refreshing morning, reduced daytime drowsiness and sense of fatigue, and higher work efficiency.

Notification No. A42

• This product is not a food for specified health use and has not been individually verified by the Secretary-General of the Consumer Affairs Agency.
• This product is not intended to diagnose, treat, or prevent disease.
• Always eat a balanced diet consisting of a staple food, main dish, and side dish.
Improving Plant and Animal Nutrition

Stimulating plant development with amino acid fertilizers

Plants require protein to grow. From absorbed nitrogen and photosynthesized glucose, they make amino acids and from those amino acids synthesize proteins. Recent research has revealed that plants also absorb amino acids directly through their roots and leaves. This means that supplying amino acids as fertilizer may facilitate protein synthesis. While research on the effects of fertilizer containing amino acids is still unfolding, their potential benefits for agricultural crops are attracting great interest.

For more than 30 years the Ajinomoto Group has been advancing efforts to effectively use the nutritionally rich by-products of amino acid fermentation (or “co-products”) as organic-type fertilizer. The Group has also been studying how to turn these co-products into balanced, value-added agricultural materials by blending them with amino acids, minerals, and other essential plant nutrients. The Group is finding that fertilizers fortified with amino acids and nucleic acids help improve root and plant growth and increase yields.

In Japan, the Group produces and markets Ajifol®

AminoGuard®, a foliar fertilizer used in the cultivation of strawberries, tomatoes, and other crops. Supplying glutamic acid through the leaves can promote growth and counteract the effects of cloudy weather and low temperatures, which hinder plant development by slowing photosynthesis.

Effect on strawberries

Before use

After use

Spraying Ajifol® AminoGuard® on the leaves of strawberries with developmental impairment thought to be caused by root damage resulted in restored vigor and improved leaf color.

Highlight Value-added fertilizers boost agricultural production in Brazil

With global population growth expected to continue, humanity’s ability to secure food over the long term is becoming a global concern. And Brazil is in a crucial position as one of the five largest agricultural crop producers in the world.

Ajinomoto Brazil wants to help solve this problem by offering solutions that boost agricultural productivity in Brazil.

AMIORGAN® and AJIFOL® are value-added fertilizers the company offers that are made using amino acid production co-products. AMIORGAN®, which contains nitrogen, potassium, and amino acids, accelerates crop development when mixed in the soil. AJIFOL® is a foliar fertilizer that supplies nutrients efficiently through the plants’ leaves.

These brands are available in a range of products designed for application at specific stages of crop development, and are suitable especially for high value-added coffee, vegetables, and fruits such as grapes, melons, and mangos.

Advantages of using AMIORGAN® and AJIFOL®

1. Higher yield
2. Stronger disease resistance
3. Sweeter fruit (Brix value)

We’ve been using Ajinomoto Group fertilizer for ten years, gradually increasing the amount because of the amazing results we’ve seen. Now we use it on all our crops. We are impressed with how this fertilizer has improved plant growth and returns.

Edison Cosmo
Brazilian producer
Feed-use amino acids promote sound growth of farm animals

High-quality animal protein obtained from edible meat is an indispensable part of the modern diet. Demand for edible meat is expected to rise in proportion to human population and economic growth, making efficient meat production an important issue for the animal industry. The use of amino acids provides a promising solution.

Farm animals are generally fed with natural feedstuffs such as corn, wheat, soybean meal, and so forth. However, feeds formulated only with these feedstuffs contain an unbalanced composition of amino acids, which leads to inefficient use of protein in the feed as well as an excess excretion of nitrogen to the environment. Adequate supplementation of necessary amino acids to the feed is widely practiced to solve this problem. This allows proteins in the natural feedstuffs to be utilized more efficiently, consequently helping the animals to grow faster and more efficiently. A significant impact of amino acid supplementation on the reduction of nitrogen load by animal excreta can also be expected.

The feed-use amino acid business of the Ajinomoto Group has more than 50 years of history. The Group has been expanding this business through science-based marketing and its unique innovative production technologies. The Ajinomoto Animal Nutrition Group has production sites in four countries and sales bases in seven countries, covering a range of businesses in the global animal nutrition field.

The “Barrel Theory” of amino acids

AjiPro®-L earns global reputation as rumen-protected lysine product

Cows, so called “ruminants,” have four stomachs, while swine and poultry have one (mono-gastric animals). Huge numbers of microorganisms live in the first stomach, the “rumen,” and help digestion by degrading cellulose, for example, which mono-gastric animals have difficulty digesting. On the other hand, indispensable nutrients such as amino acids are also degraded in this process, so that the nutrients don’t reach the small intestine where absorption occurs. Recently, as the productivity of dairy cows improves, demand for a technology that protects amino acids from degradation in the rumen and delivers them in an intact form to the small intestine has been rising substantially.

In order to solve this problem, the Ajinomoto Group developed AjiPro®-L and launched it in North America in 2011. AjiPro®-L is a rumen-protected lysine for dairy cows that, using unique processing technology, delivers lysine to the intestine without being degraded in the rumen.

AjiPro®-L has a high reputation in the dairy industry and is now the leading product of rumen-protected lysine for dairy cows in North America. The Ajinomoto Group is also poised to launch the product in Asia, the Middle East, and Oceania. Sales have already begun in Japan in April 2015 where seminars were held for dairy farmers to broadly communicate the product’s effectiveness.

Method developed for measuring available lysine content

Daily cows are fed AjiPro®-L and the rate of absorption in the small intestine is calculated. AjiPro®-L is released from the small intestine and absorbed in the small intestine.
Basic and applied research driving the future of electronic materials business

Amino acid technology spawned a ubiquitous electronic material

The Ajinomoto Group has been in the electronic materials business since 1996. Starting with research into the potential uses of by-products of the AJI-NO-MOTO® manufacturing process, these efforts produced curing agents, adhesives, and other materials—expanding research in the field of resins and inks in the process.

Insulating film “Ajinomoto Build-up Film” (ABF), released in 1999, boasts a sizable share of the global market as an insulating material for CPUs, the core component of personal computers. In 1996, prior to its release, CPU insulating materials existed only in liquid form, posing drawbacks such as easy adherence of dust and an often uneven finish. To meet manufacturers’ needs for a film-type insulating material, the Group commenced research and development and in one year succeeded. An increasing number of manufacturers adopted the film, eventually making it the industry standard.

Combining its cutting-edge ABF and amino acid technologies, the Group is also working on Organic Light Emitting Diodes (OLEDs), a new field with exciting environmental implications.

One area the Group is focused on is materials for OLED devices. OLED materials present numerous advantages for adoption in lighting and displays: they are thin and light; emit a soft light as an area light source; generate little heat, making them suitable for products sensitive to heat; and have a high level of design versatility.

Previously, the light emitting portion of OLED devices needed to be encapsulated in glass to completely insulate them from ambient air. This posed problems in terms of cost, vulnerability to impacts, and rigidity.

To address these issues, Ajinomoto Fine-Techno Co., Inc. developed Ajinomoto Encapsulation Film (AEF). This film, which adheres to the light emitting portion to protect it from oxygen and moisture, offers superior design characteristics, being thin, light, transparent, and bendable, while also simplifying the OLED device manufacturing process to reduce costs.

If AEF is adopted by lighting component and display manufacturers, it could open up new possibilities across a vast array of industries—from consumer electronics and digital signage, to clothing and fashion, building materials, disaster preparedness, and healthcare. Ajinomoto Fine-Techno Co., Inc. is partnering with such manufacturers to make these possibilities a reality.

Potential OLED applications

**Digital signage**
Lightweight, bendable signs could adorn columns and building walls

**Light fixtures**
Light surfaces could be bent into stylish shapes or wrapped over complex forms, such as car interiors

**Refrigerated display cases**
Lower heat and zero UV generation could help prevent food quality deterioration

Yuichi Kageyama, PhD
Group Manager, R&D Department, Ajinomoto Fine-Techno Co., Inc.

OLED materials have a low environmental impact: They’re energy efficient, greatly helping to reduce carbon dioxide gas emissions. They contain no mercury or other harmful chemicals like fluorescent bulbs, making them recycle friendly. I have two daughters, and as I watch them grow up happily I am reminded that I don’t want to leave behind a more polluted global environment. If only the materials we develop could help create a cleaner future for our children—that’s the mindset that drives my work on this project.