Physiological Functions of Proteinogenic Amino Acid

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Summary The symposium entitled “Physiological Functions of Proteinogenic Amino Acid” is being held at the 22nd IUNS-ICN International Congress of Nutrition in December 2022 in Tokyo, Japan. The symposium is cochaired by Dr. Shigeki Furuya from Kyushu University and Dr. Tsutomu Fukuwatari from The University of Shiga Prefecture, co-organized by the International Council on Amino Acid Science and Japanese Society for Amino Acid Sciences. In recent years, amino acid researchers have made great strides in finding the physiological functions of proteinogenic amino acids and their metabolites, and opened a new era for amino acid and nutritional sciences. The goal of this symposium is to highlight the novel and important physiological function of proteinogenic amino acids from nutritional aspects. This amino acids symposium features 4 speakers, each presenting novel insights into mechanisms by which amino acids participate in brain function, diabetes, taste functions and energy metabolism, respectively. Dr. Gilles Bonvento from University Paris-Saclay/CNRS/CEA talks about the role of serine in brain function. Dr. Ara Koh from Pohang University of Science and Technology, POSTECH, presents histidine-derived microbial imidazole propionate in diabetes. Dr. Hisayuki Uneyama from Ajinomoto Co., Inc., talks about taste functions of amino acids for improving health and wellbeing. Dr. Jorge L. Ruas from Karolinska Institute describes the tryptophan-kynurenine pathway in the regulation of energy metabolism.

Key Words amino acid, brain function, diabetes, energy metabolism, taste function

Amino acids are defined as organic compounds containing both an amino group and a carboxyl group in the same molecule, and thousands of compounds correspond to amino acids. Only 23 amino acids are incorporated into proteins during translation, and are thus known as “proteinogenic amino acids”. Generally known physiological functions of proteinogenic amino acids are components of proteins and peptides, contribution to proteins structure, precursors of glucose, ketone bodies and nitrogen-containing molecules, modulation of various biological activities as signal molecules, and regulators of osmotic pressure. In recent years, amino acids researchers have made great strides in finding the physiological functions of proteinogenic amino acids and their metabolites, and opened a new era for amino acid and nutritional sciences. This symposium titled “Physiological Functions of Proteinogenic Amino Acid” is one of the special feature programs at the 22nd IUNS-ICN International Congress of Nutrition held in December 2022 in Tokyo, Japan. The symposium is co-organized by the International Council on Amino Acid Science (ICAAS) and Japanese Society for Amino Acid Sciences (JSAAS). The former explores scientific issues related to the intake of appropriate amounts of amino acids as food or dietary ingredients, and was established with the aim of contributing to health promotion and dietary improvement. The latter was founded to contribute advancement and dissemination in amino acid sciences through providing and exchanging information on amino acid sciences. This amino acids symposium features 4 speakers, each presenting novel insights into mechanisms by which amino acids participate in brain function, diabetes, taste functions and energy metabolism, respectively. The goal of this symposium is to highlight the novel and important physiological functions of proteinogenic amino acids from nutritional aspects.

The first speaker, Dr. Gilles Bonvento from Université Paris-Saclay, CEA, CNRS, MIRCen, Laboratoire des Maladies Neurodégénératives, France, has been interested in energy metabolism abnormalities and higher dysfunction in age-related neurodegenerative diseases and their pathogenic mechanisms. As a neuroscientist, his research is characterized by focusing on the functional and metabolic interaction between neurons and astrocytes, a type of glial cell in the brain. His group has applied novel imaging techniques of metabolite sensors, along with physiological and behavioral analyses, to animal models of neurodegenerative diseases. He has studied a mechanistical link between impaired brain metabolism and degenerative diseases, and recently made new discoveries regarding the pathobiological significance of metabolic alteration of l-serine in Alzheimer’s disease (1) An international research team led by

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him found that in an Alzheimer’s disease model, a reduction in the glycolytic system, particularly in the hippocampus, is responsible for reduced neuroplasticity via diminished L-serine level, which leads to impaired spatial memory learning, and that oral L-serine intake can ameliorate these impairments. Importantly, his team provided evidence that these pathological changes also occur in human Alzheimer’s patients. Recently, he and his colleagues also reviewed past and recent findings on the neurobiological significance of astrocytic serine metabolism (2). These topics will be presented in his talk.

Dr. Ara Koh from Pohang University of Science and Technology, POSTECH, Korea, talks about histidine-derived microbial imidazole propionate. Increasing evidence indicates that interactions between the gut microbiota, diet, and the host contribute to the development of metabolic diseases such as type 2 diabetes. Dr. Koh found that type 2 diabetes patients show higher plasma imidazole propionate, a microbially produced histidine-derived metabolite. Administration of imidazole propionate impairs glucose tolerance, and this is because imidazole propionate impairs insulin signaling at the level of insulin receptor substrate through the activation of p38 MAPK, which promotes p62 phosphorylation and, subsequently, activation of the mechanistic target of rapamycin complex 1 (mTORC1) (3).

Although metformin is the first-line therapy for type 2 diabetes, there are large inter-individual variations in responses to this drug. She found that in type 2 diabetes patients taking metformin who have high blood glucose, pretreatment with imidazole propionate attenuates the metformin-induced glucose lowering effect, and imidazole propionate inhibits AMP-activated protein kinase (AMPK) activation by activating p38γ/Akt. Blocking imidazole propionate-induced p38γ activation is effective to lower blood glucose levels with metformin in vivo (4). The fecal microbiota of the patients has increased capacity to produce imidazole propionate, which is mediated by the bacterial enzyme urocanate reductase. She determined the X-ray structures of the ligand-binding domains of bacterial urocanate reductase. This analysis provides a useful tool for structure-based drug design for designing inhibitors for future treatment of type 2 diabetes (5).

The third speaker, Dr. Hisayuki Uneyama, has been engaged in pharmaceutical research at the Institute of Biological Chemistry, Ajinomoto Co., Inc., and then in food research, particularly in the nutritional physiology of amino acids. He is currently an Executive Specialist in the Global Communications Department. His research has focused on the physiological role of chemosensory cues presented by the umami taste of glutamate. His research group found that the gastric vagus nerve responds to free glutamate to recognize food intake and initiate digestion (6–9). In vivo observations clearly indicate that the glutamate signal from the stomach activates specific neurons in the hypothalamus and that physiological responses such as meal-induced heat production are modulated via this gut-brain axis.

Recently, it is becoming clear that glutamate in food not only brings out the deliciousness of food as umami taste, but is also a food signal that stimulates saliva secretion during chewing, facilitates swallowing, and acts on the gastrointestinal tract to help digestion and absorption of food. Current attempts have been made to utilize these nutritional and physiological actions of umami taste for promoting health and longevity. The histological overview with the latest findings on the taste functions of amino acids, especially glutamate, will be presented in his talk.

The final presentation, “The tryptophan-kynurenine pathway in the regulation of energy metabolism” is given by Dr. Jorge L Ruas from Karolinska Institute, Sweden. The kynurenine pathway of tryptophan degradation generates metabolites with effects on metabolism, immunity, and mental health, and thus understanding the regulation of the kynurenine pathway is an area of great interest for a growing number of scientific fields such as oncology, immunology, psychiatry, and metabolism (9). Dr. Ruas found that the skeletal muscle can be a target to regulate the kynurenine pathway, and endurance training can change the pathway by inducing the expression of the pathway enzyme in skeletal muscle. He first showed that the activation of skeletal muscle peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α) increases skeletal muscle expression of kynurenine aminotransferases, which enhances the conversion of kynurenine into kynurenic acid. Enhancement of kynurenine aminotransferases expression reduces plasma kynurenine levels, and protects the brain from depression induced by chronic mild stress or direct kynurenine administration (10). Exercise-induced kynurenine aminotransferase expression also increases the conversion of 2-oxoglutarate to glutamate in the malate-aspartate shuttle, improving energy utilization and the transfer of fuel-derived electrons to mitochondrial respiration (11). He further demonstrated that aerobic exercise training increases plasma kynurenic acid levels, and circulating kynurenic acid increases energy utilization by activating G protein-coupled receptor GPR35, which stimulates lipid metabolism, and thermogenic and anti-inflammatory gene expression in adipose tissue. Kynurenic acid and GPR35 enhance PGC-1α expression and cellular respiration, leading to enhancement of β-adrenergic receptor signaling (12).

This review was written by two organizers in March 2022, prior to the symposium. Responsibility for the content rests with these two organizers.

Disclosure of state of COI
No conflicts of interest to be declared.

REFERENCES


