*Forum Minireview***New Therapeutic Strategy for Amino Acid Medicine:
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Amino acids are fundamental materials composing our body protein and life activities, and they have two distinct aspects, nutritional and physiological functions within our body. For medical use of amino acids, we know a variety of amino acid elemental diets, such as the Elental liquid diet, that effectively supply essential amino acids without digestion, and they have been used based on their nutritional benefits (1). In contrast, behind the recent health trend in utilizing amino acids, the physiological function specific for each amino acid has been extensively investigated and investigators have tried to use this information to develop suitable amino acid preparations for medical treatment. The most famous amino acid may be glutamine, for which a therapeutic effect was originally discovered by Okabe and Takeuchi (2). Now, glutamine is well known as a functional amino acid in clinics to treat gastrointestinal mucosal disorders (3). Discoveries of amino acid transporters and specific receptors in the brain, gut, kidney, and skeletal muscle have suggested those molecules as therapeutic targets and accelerated the application of the amino acid itself for medicine. We have summarized recent trials in amino acid medicine in Table 1.

Nonessential amino acid glutamate and glycine are known to act as major neurotransmitters within the brain. Recently, receptors recognizing glutamate and glycine were identified in the peripheral tissues such as taste and

digestive organs (4 – 6). It has been reported that supplementation of glutamate improved gastrointestinal functions (motility and mucus secretion), leading to the hypothesis that glutamate may prevent gastro-duodenal ulcer and functional dyspepsia (7, 8). Bannai et al. has clearly suggested that glycine intake before bedtime can improve the quality of sleep and glycine could be used as a medicine for patients with sleep disorders (9). Clinical evidence for the effectiveness of essential amino acids, branched chain amino acids (BCAAs, for treating sarcopenia in the elderly has been accumulated as well (10).

At the 84th Annual Meeting of The Japanese Pharmacological Society, Yokohama, March 2011, we held a symposium to review issues associated with current therapeutic strategy of new amino acid medicine. As the proceedings of our symposium, we chose typical candidates for functional amino acids (glutamine, glutamic acid, glycine, BCAA) and discussed their possible clinical use to prevent or treat gastrointestinal, eating, and sleep disorders and muscle sarcopenia (11 – 14). We hope this Forum Minireview series will prompt investigators to start thinking of new strategies for amino acid medicine.

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Table 1. Major functional amino acids for clinical use

Amino acids	Possible mechanisms	Possible targets (symptom/disease)
Essential amino acids		
BCAA (Leu, Ileu, Val)	mTOR activation/essential nutrients	post-operative enteral/parental nutrition, Crohn's disease, sarcopenia, hyperammonemia, hypoalbuminemia, chronic hepatic disease
Lysine	unknown/essential nutrients	herpes simplex virus, stress syndrome, anxiety
Tryptophan	monoamine precursors	sleep disorder, anxiety
Methionine	unknown/essential nutrients	chronic hepatic disease
Nonessential amino acid		
Glutamine	intracellular glutamate precursor/nutrient	post-operative enteral/parental nutrition, gastrointestinal ulcers, oral cares during cancer therapy, gastritis
Arginine	nitric oxide (NO) precursor/nutrient	post-operative enteral/parental nutrition, oral cares during cancer therapy, hyperammonemia, inborn urea cycle disorder
Glutamic acid	regulation of gastrointestinal functions (motility and exocrine reflexes) via gut glutamate receptors/gut nutrients	post-operative enteral/parental nutrition, gastrointestinal ulcers, hyperammonemia, oral cares during cancer therapy, gastritis, eating disorders, dyspepsia, functional dyspepsia
Glycine	central and peripheral glycine receptors/anti-inflammatory effects	gastro-esophageal reflux disease, chronic hepatic disease, schizophrenia, sleep disorder, dysuria
Alanine	unknown/peripheral glycine receptor/nutrient	benign prostatic hyperplasia, dysuria, chronic hepatic disease

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