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AMINO ACIDS: FUNDAMENTAL BIOMOLECULES TO METABOLIC REGULATORS AND THERAPEUTIC TARGETS IN HUMAN HEALTH AND DISEASE

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ABSTRACT
Amino acids are indispensable biological molecules that traditionally have been recognized as the fundamental building blocks of proteins. Contemporary research, however, has established that their biological functions extend considerably beyond protein synthesis. Amino acids participate in energy production, nitrogen homeostasis, redox regulation, neurotransmitter synthesis, immune responses, epigenetic regulation and intracellular signaling. Their metabolism is closely integrated with carbohydrate and lipid metabolism and contributes to the maintenance of cellular and systemic homeostasis. Deregulations of amino acid availability, transport and catabolism has increasingly been associated with metabolic, cardiovascular, renal, immune and malignant diseases.
The present review provides an integrated overview of amino acid structure, classification, nutritional significance, digestion, absorption, transport and metabolic utilization, with particular emphasis on their emerging role as metabolic regulators. The review discusses essential, non-essential and conditionally essential amino acids, glucogenic and ketogenic amino acids, branched-chain amino acids (BCAAs), one-carbon metabolism, the urea cycle and amino-acid-dependent signaling pathways. Particular attention is given to glutamine, glutamate, arginine, methionine, glycine, serine, tryptophan and BCAAs because of their increasingly recognized roles in human disease.
Recent evidence indicates that cancer cells undergo extensive amino acid metabolic reprogramming to support proliferation, biosynthesis, redox homeostasis and immune escape. Amino acid availability can influence tumor growth through nutrient-sensing pathways including mTOR signaling, while amino acid transporters and metabolic enzymes represent potential therapeutic targets. Similarly, altered BCAA metabolism has been associated with insulin resistance, diabetes and cardiovascular disease, although causal relationships may differ among individual amino acids and disease contexts. The kidney is also a major organ in amino acid synthesis, degradation, filtration, reabsorption and nitrogen handling, making amino acid metabolism particularly relevant to chronic and diabetic kidney diseases.
Collectively, current evidence supports a transition from viewing amino acids merely as nutritional substrates toward understanding them as dynamic metabolic signals and potential biomarkers and therapeutic targets. Future research integrating metabolomics, stable-isotope tracing, multi-omics approaches and precision nutrition may help translate amino acid biology into personalized strategies for disease prevention and treatment.

KEYWORDS: Amino acids; amino acid metabolism; branched-chain amino acids; glutamine; mTOR; cancer metabolism; diabetes; cardiovascular disease; kidney disease; metabolomics; precision nutrition; therapeutic targets.

INTRODUCTION

Amino acids constitute one of the most fundamental classes of biomolecules in living systems. They are required for protein synthesis and therefore participate directly in the formation of enzymes, receptors, transporters, structural proteins, antibodies and numerous regulatory molecules. Nevertheless, the biological importance of amino acids extends well beyond their incorporation into proteins. Individual amino acids and their metabolites function as substrates, signaling molecules, neurotransmitter precursors, nitrogen donors, redox regulators and intermediates in biosynthetic pathways.
Amino acid metabolism is integrated with virtually every major metabolic network. Carbon skeletons generated from amino acid catabolism can enter the tricarboxylic acid (TCA) cycle, gluconeogenesis or ketogenesis, whereas amino groups contribute to nitrogen metabolism and ultimately urea formation. Several amino acids also provide one-carbon units, reducing equivalents and precursors for nucleotides, lipids, neurotransmitters and antioxidant systems.
The modern concept of amino acid metabolism has therefore expanded from a simple nutritional framework to a systems-level understanding of metabolic regulation. Amino acid homeostasis is controlled through dietary intake,

endogenous protein turnover, de novo synthesis, tissue-specific catabolism, transport and renal/hepatic clearance. Disruption of any of these processes may affect cellular function and disease susceptibility.

A comprehensive 2023 review emphasized that abnormal amino acid metabolism is associated with metabolic diseases, cardiovascular diseases, immune disorders and cancer. More recent research has further demonstrated disease-specific alterations in amino acid metabolism and has raised the possibility of using amino acid-related pathways as diagnostic biomarkers or therapeutic targets.

The emerging importance of amino acids is particularly evident in cancer biology. Malignant cells frequently reprogram amino acid uptake and utilization to satisfy increased demands for biomass production, energy metabolism, redox protection and signaling. Importantly, this metabolic phenotype is heterogeneous: different cancers, and even different regions of the same tumor, may display distinct amino acid dependencies.

Similarly, BCAA metabolism has attracted substantial attention in cardiometabolic research. Leucine, isoleucine and valine are essential amino acids that participate in protein synthesis and nutrient sensing, but altered circulating concentrations and impaired catabolism have also been associated with insulin resistance and cardiovascular disease.

The kidney represents another important metabolic organ. It contributes to amino acid synthesis, degradation, reabsorption, excretion, gluconeogenesis and nitrogen handling. Consequently, renal dysfunction can substantially alter systemic amino acid concentrations and metabolic pathways.

The objective of this review is to provide an integrated and updated perspective on amino acid biology, emphasizing the transition from their classical biochemical functions to their emerging roles in disease mechanisms, biomarkers, metabolic signaling and therapeutic intervention.

2. Chemical Structure and General Properties

Amino acids generally contain an amino group, a carboxyl group, a hydrogen atom and a variable side chain attached to a central α-carbon. The side chain determines the chemical and biological properties of each amino acid.

At physiological pH, amino acids commonly exist as zwitterions, carrying both positive and negative charges. Their ionization properties influence protein structure, enzyme activity and membrane transport and biochemical interactions.

The stereochemistry of amino acids is also biologically important. Most proteinogenic amino acids occur predominantly in the L-configuration in proteins, although D-amino acids occur in selected biological systems and microorganisms.

The side-chain structure provides the basis for classifying amino acids according to polarity, charge, aromaticity, sulfur content and metabolic fate.

3. Classification of Amino Acids

Essential amino acids	Non-essential amino acids
Histidine	Alanine
Isoleucine	Arginine
Leucine	Asparagine
Lysine	Aspartic acid
Methionine	Cysteine
Phenylalanine	Glutamic acid
Threonine	Glutamine
Tryptophan	Glycine
Valine	Proline
	Serine
	Tyrosine

3.1 Essential Amino Acids

Essential amino acids cannot be synthesized by humans in sufficient quantities and therefore must be supplied through the diet.

Their dietary availability is particularly important during growth, pregnancy, illness and other physiological states characterized by increased metabolic requirements.

3.2 Non-essential Amino Acids

Non-essential amino acids can generally be synthesized endogenously.
However, the designation “non-essential” does not mean that these amino acids are biologically unimportant.

3.3 Conditionally Essential Amino Acids

Some amino acids become conditionally essential when endogenous synthesis is insufficient relative to physiological demand. Arginine, glutamine, cystine, glycine, proline and tyrosine may become particularly important during growth, severe illness, trauma or metabolic stress.

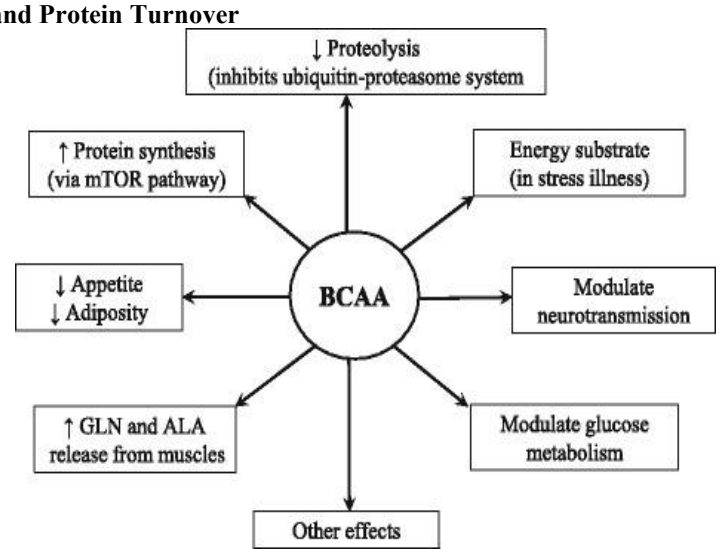
4. Proteinogenic and Non-proteinogenic Amino Acids

- The canonical genetic code incorporates 20 amino acids into proteins. These proteinogenic amino acids form the basis of the human proteome.
- In addition, numerous non-proteinogenic amino acids participate in biological processes. Examples include ornithine, citrulline, taurine and γ-aminobutyric acid (GABA).
- Several non-proteinogenic amino acids are metabolic intermediates rather than structural components of proteins. Ornithine and citrulline, for example, are central to the urea cycle.

5. Digestion, Absorption and Transport

- Dietary proteins undergo digestion in the gastrointestinal tract through gastric and pancreatic proteases. Peptides and free amino acids are subsequently absorbed predominantly in the small intestine.
- Amino acid transport is mediated by multiple transporter systems. These transporters determine cellular availability and influence metabolic signaling.
- Transport is particularly important in cancer biology because malignant cells may increase expression of selected amino acid transporters to satisfy increased nutritional requirements. Abnormal amino acid transport can therefore contribute to metabolic reprogramming and may provide a therapeutic opportunity.

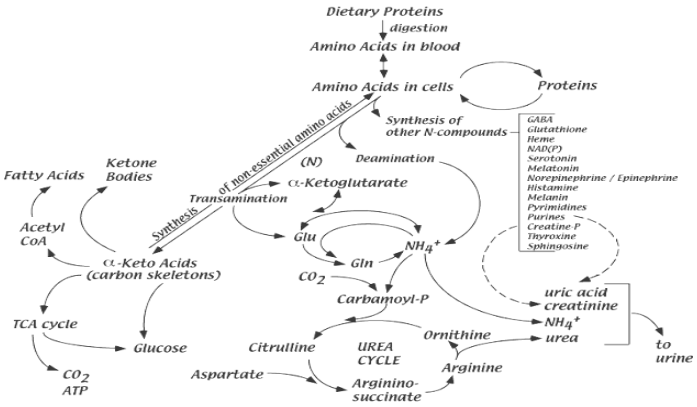
6. Amino Acid Pool and Protein Turnover



- The human body maintains a dynamic amino acid pool derived from dietary intake, protein degradation and endogenous synthesis.
- Proteins are continuously synthesized and degraded. This process, termed protein turnover, permits tissue remodeling and provides amino acids for metabolic requirements.
- During fasting or severe metabolic stress, increased proteolysis can release amino acids that support gluconeogenesis and energy production. Conversely, adequate amino acid availability stimulates anabolic pathways and protein synthesis.
- Leucine is particularly important as a nutrient signal because amino acid availability can activate mechanistic target of rapamycin complex 1 (mTORC1), a major regulator of cellular growth and protein synthesis.

7. Metabolism of Amino Acids

Amino acid catabolism involves separation and subsequent utilization of the amino and carbon components.



7.1 Transamination

- Transamination transfers an amino group from an amino acid to an α-keto acid. Aminotransferases play central roles in this process.
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are clinically important enzymes because their circulating concentrations can reflect tissue injury, particularly hepatic injury.

7.2 Oxidative Deamination

- Glutamate occupies a central position in nitrogen metabolism. Oxidative deamination of glutamate produces α-ketoglutarate and ammonia.
- The resulting α-ketoglutarate can enter the TCA cycle, thereby linking amino acid metabolism with energy metabolism.

7.3 Urea Cycle

Ammonia generated during amino acid catabolism is toxic, particularly to the central nervous system. The liver converts ammonia into urea through the urea cycle, allowing nitrogen to be safely excreted.

The principal urea-cycle intermediates include:

- Carbamoyl phosphate
- Citrulline
- Argininosuccinate
- Arginine
- Ornithine
- Disruption of this pathway can cause hyperammonaemia and serious neurological consequences.

8. Glucogenic and Ketogenic Amino Acids

- Amino acids can be classified according to the metabolic fate of their carbon skeletons.
- Glucogenic amino acids generate intermediates that can contribute to gluconeogenesis.
- Ketogenic amino acids generate acetyl-CoA or acetoacetate and therefore contribute to ketone-body formation.
- Leucine and lysine are considered exclusively ketogenic amino acids, whereas several other amino acids possess both glucogenic and ketogenic characteristics.
- This classification demonstrates the close metabolic relationship between amino acids, glucose and lipid metabolism.

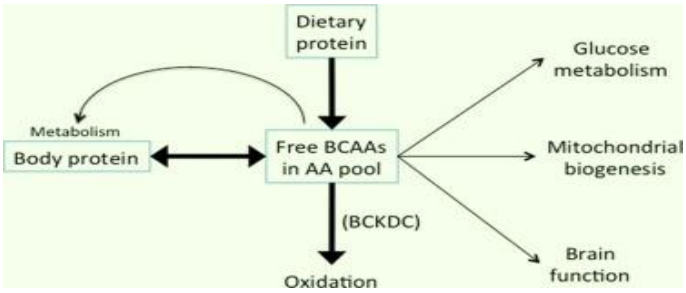
9. Branched-Chain Amino Acids

The BCAAs—leucine, isoleucine and valine—are essential amino acids with a branched aliphatic side chain.

Unlike many amino acids, substantial BCAA catabolism occurs in extrahepatic tissues, particularly skeletal muscle.

BCAA metabolism involves:

- Branched-chain aminotransferase (BCAT)
- Branched-chain α-keto acid dehydrogenase (BCKDH)



- Subsequent oxidation of carbon skeletons

BCAAs are also important nutrient signals. Leucine can stimulate mTORC1 signaling and promote protein synthesis.
However, elevated circulating BCAAs have been repeatedly associated with cardiometabolic disorders. Current evidence suggests that the relationship is complex and cannot simply be interpreted as "BCAAs are harmful." Experimental and genetic studies indicate that individual BCAAs may exert distinct or even opposing effects.

10. Glutamine and Glutamate Metabolism

- Glutamine is one of the most abundant amino acids in human plasma and plays multiple roles in nitrogen transport, nucleotide synthesis, redox regulation and energy metabolism.
- Glutaminolysis converts glutamine to glutamate through glutaminase. Glutamate can subsequently generate α-ketoglutarate and contribute to the TCA cycle.
- In proliferating cells, glutamine may provide carbon and nitrogen for biosynthetic processes. This is especially relevant to tumor cells.
- Cancer cells can exhibit enhanced glutamine uptake and utilization, although glutamine dependency varies considerably among tumor types and environmental conditions. Modern research increasingly emphasizes metabolic heterogeneity rather than assuming universal glutamine addiction.

11. Methionine and One-Carbon Metabolism

- Methionine is an essential sulfur-containing amino acid that contributes to methyl-group metabolism.
- Methionine is converted into S-adenosylmethionine (SAM), a major methyl donor involved in DNA, RNA, protein and lipid methylation.
- After methyl-group transfer, SAM is converted to S-adenosylhomocysteine and subsequently homocysteine.
- The methionine cycle is closely interconnected with folate-mediated one-carbon metabolism and therefore influences epigenetic regulation.
- Dysregulated methionine metabolism has attracted interest in cancer research because malignant cells may demonstrate altered methylation requirements and methionine dependence.

12. Serine, Glycine and One-Carbon Metabolism

Serine and glycine participate in one-carbon metabolism and nucleotide biosynthesis.
Serine can be converted into glycine while donating one-carbon units to tetrahydrofolate-dependent reactions.
This pathway supports:

- Purine synthesis
- Thymidylate synthesis
- Methylation reactions
- Redox metabolism

Rapidly proliferating cells can increase their demand for serine and glycine because of increased requirements for nucleotide synthesis and biomass production.

13. Arginine and Nitric Oxide Metabolism

Arginine participates in the urea cycle and is also the substrate for nitric oxide synthase.
Nitric oxide is an important signaling molecule involved in vascular relaxation, platelet function, immune regulation and cellular signaling.
Arginine metabolism therefore connects nitrogen metabolism with cardiovascular physiology and immune responses.
Disruption of arginine availability or nitric oxide production may contribute to endothelial dysfunction and inflammatory processes.

14. Tryptophan Metabolism

- Tryptophan is an essential aromatic amino acid and precursor of several biologically active compounds.

- It contributes to the synthesis of serotonin and melatonin and is also metabolized through the kynurenine pathway.
- The kynurenine pathway generates metabolites that influence immune responses, neurological function and cellular metabolism.
- Altered tryptophan metabolism has received increasing attention in cancer and immune regulation because tumor and immune cells can compete for or modify tryptophan availability.

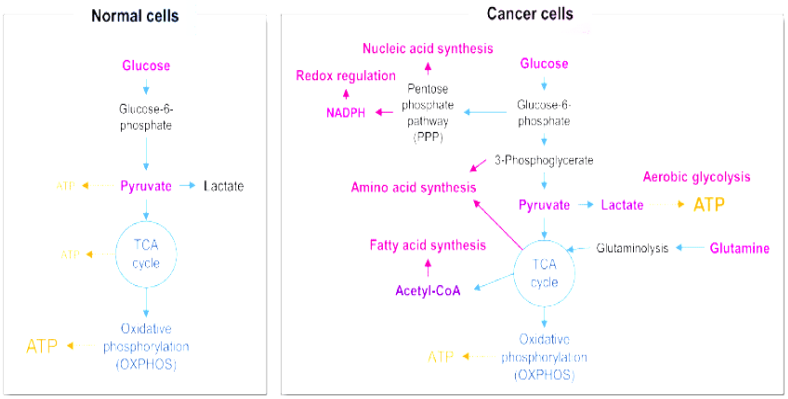
15. Amino Acids, Oxidative Stress and Redox Homeostasis

- Amino acids contribute substantially to cellular antioxidant defense.
- Glutamate, cysteine and glycine are required for glutathione synthesis.
- Glutathione is a major intracellular antioxidant and protects cells against reactive oxygen species.
- Cysteine availability can therefore influence cellular redox status. This pathway is particularly important in cancer cells, which often experience substantial oxidative stress due to rapid proliferation and altered mitochondrial metabolism.
- Amino acid metabolism is consequently closely connected with ferroptosis, a form of regulated cell death involving iron-dependent lipid peroxidation.

16. Amino Acid Metabolism in Cancer

Cancer is characterized by profound metabolic reprogramming. Although glucose metabolism has traditionally received major attention, amino acid metabolism is now recognized as an equally important component of tumor biology.

Tumor cells may alter:



- Amino acid uptake
- Amino acid synthesis
- Amino acid degradation
- Amino acid transport
- Nitrogen metabolism
- Redox metabolism
- Nutrient-sensing signaling

Amino acids support tumor growth by providing substrates for protein synthesis, nucleotide production, energy metabolism and antioxidant defense.

Recent reviews emphasize that amino acid metabolism can also influence tumor immunity and epigenetic regulation.

16.1 Glutamine Dependency

Glutamine may support anaplerosis, nucleotide biosynthesis and redox homeostasis.

Glutaminase inhibitors and other approaches targeting glutamine metabolism have therefore been investigated as anticancer strategies.

16.2 Asparagine Metabolism

Asparagine metabolism has a particularly important therapeutic history because asparaginase-mediated depletion of circulating asparagine is an established component of treatment for acute lymphoblastic leukemia.

16.3 Arginine Metabolism

Some tumors exhibit limited capacity for endogenous arginine synthesis and may therefore become dependent on extracellular arginine.

This has encouraged investigation of arginine-depletion approaches.

16.4 Methionine Metabolism

Methionine dependence has been observed in several experimental cancer models. Methionine metabolism may influence methylation, proliferation and redox homeostasis.

16.5 Amino Acid Transporters
Transporters including systems associated with glutamine and cystine uptake are increasingly recognized as potential therapeutic targets.
However, metabolic redundancy and tumor heterogeneity represent major challenges.

17. Amino Acid Metabolism and Tumor Immunity
Amino acids are not utilized only by tumor cells. Immune cells also require amino acids for proliferation, differentiation and effectors function.
Within the tumor microenvironment, competition for nutrients can alter immune-cell activity.
For example, depletion of specific amino acids may impair T-cell function, whereas altered tryptophan and arginine metabolism can contribute to immune suppression.
Thus, targeting amino acid metabolism must consider both tumor cells and the immune microenvironment.
Recent literature emphasizes the importance of metabolic heterogeneity within tumors and the need for context-specific therapeutic approaches.

18. Amino Acids in Diabetes and Metabolic Syndrome
Altered amino acid concentrations are frequently observed in metabolic disorders.
BCAA elevation has been associated with insulin resistance and type 2 diabetes in numerous observational studies.
Potential mechanisms include:
- Impaired BCAA oxidation
- Accumulation of branched-chain keto acids
- Altered mTOR signaling
- Mitochondrial dysfunction
- Lipid accumulation
- Inflammatory signaling

A 2023 study reported increased serum BCAAs in individuals with type 2 diabetes and an association with atherosclerotic cardiovascular disease.
Nevertheless, association does not necessarily establish causality. Genetic and experimental evidence indicates that individual BCAAs may have different metabolic effects.
Consequently, amino acid profiles may have potential as biomarkers of metabolic dysfunction, but clinical interpretation requires consideration of diet, obesity, physical activity, renal function and other metabolic variables.

19. Amino Acids in Cardiovascular Disease
Amino acid metabolism has emerged as an important component of cardiovascular biology.
BCAAs, arginine, glycine and aromatic amino acids have been investigated in relation to:
- Atherosclerosis
- Hypertension
- Myocardial ischemia
- Heart failure
- Endothelial dysfunction
- Insulin resistance

BCAA dysregulation has been linked to cardiovascular disease through effects on mitochondrial metabolism, lipid metabolism, inflammatory pathways and nutrient sensing.
Arginine metabolism is particularly important because nitric oxide production contributes to vascular homeostasis.
Amino acid-derived metabolites may therefore represent potential biomarkers and therapeutic targets in cardiovascular disease.

20. Amino Acid Metabolism in Kidney Health and Disease

The kidney is a central organ of amino acid homeostasis.
Renal functions include:
- Filtration
- Reabsorption
- Excretion
- Amino acid synthesis
- Amino acid degradation
- Gluconeogenesis
- Nitrogen handling

- Acid-base regulation

The kidney also contributes to systemic metabolic homeostasis through the metabolism of glutamine and other amino acids.
Chronic kidney disease can substantially alter circulating amino acid concentrations and amino acid metabolism. The relationship is bidirectional: kidney dysfunction alters amino acid metabolism, while abnormal metabolites may contribute to disease progression.
A 2024 Nature Reviews Nephrology review highlighted the kidney as an underappreciated metabolic hub for amino acid metabolism and described potential implications for dietary and pharmacological intervention.
Diabetic kidney disease has also been linked with alterations in BCAA metabolism, urea-cycle-related amino acids and crenitine metabolism.

21. Amino Acids as Biomarkers

Metabolomics has created new opportunities to study amino acid profiles in human disease.
Potential applications include:

- Early disease detection
- Disease classification
- Prognostic assessment
- Treatment-response monitoring
- Identification of metabolic phenotypes

BCAAs and aromatic amino acids have been investigated as metabolic biomarkers, particularly in cardiometabolic and hepatic disorders.
However, biomarker development requires large, well-characterized cohorts, standardized analytical methods and independent validation.

22. Amino Acids and Precision Nutrition

Precision nutrition aims to tailor dietary recommendations according to individual biological characteristics.
Amino acid metabolism is particularly suitable for precision nutrition because amino acid requirements are influenced by:

- Age
- Sex
- Physical activity
- Disease state
- Renal function
- Liver function
- Microbiome
- Genetic variation

Overall dietary composition
Future nutritional strategies may therefore move beyond generalized protein recommendations toward individualized amino acid requirements.

23. Therapeutic Applications

Several strategies are being investigated to manipulate amino acid metabolism therapeutically.

23.1 Amino Acid Depletion

Enzymatic depletion of selected amino acids can create metabolic stress in tumor cells.

23.2 Transporter Inhibition

Blocking amino acid transport may reduce intracellular nutrient availability.

23.3 Metabolic Enzyme Inhibition

Inhibiting glutaminase, amino acid biosynthetic enzymes or catabolic pathways may selectively affect metabolically vulnerable cells.

23.4 Dietary Manipulation

Controlled modification of dietary amino acid availability has been proposed for selected diseases. However, aggressive dietary restriction can also cause malnutrition and loss of lean mass, particularly in patients with cancer or chronic disease.

23.5 Combination Therapy

Amino acid metabolic inhibitors may potentially be combined with chemotherapy, targeted therapy or immunotherapy.
Recent literature emphasizes that therapeutic targeting must account for metabolic plasticity and treatment resistance.

24. Current Challenges

Despite major advances, several important questions remain unresolved.

First, amino acid metabolism is highly tissue-specific. A metabolic alteration beneficial in one tissue may be harmful in another.
Second, circulating amino acid concentrations do not always accurately reflect intracellular metabolism.
Third, observational associations cannot automatically be interpreted as causal relationships.
Fourth, metabolic pathways exhibit substantial redundancy. Blocking one pathway may result in metabolic adaptation through alternative pathways.
Fifth, nutritional interventions must balance therapeutic metabolic effects against the risk of protein-energy malnutrition.
Finally, cancer metabolism is heterogeneous. A strategy effective against one tumor subtype may be ineffective in another.

25. Future Perspectives
Future amino acid research will increasingly depend on integrated multi-omics approaches.
Important technologies include:

- Targeted metabolomics
- Untargeted metabolomics
- Stable-isotope tracing
- Transcriptomics
- Proteomics
- Single-cell sequencing
- Spatial metabolomics
- Artificial intelligence
- Machine learning

Stable-isotope tracing may be particularly valuable because it allows investigators to determine how amino acid carbon and nitrogen atoms move through metabolic pathways rather than simply measuring metabolite concentrations.
In oncology, spatial metabolomics may help reveal metabolic differences between tumor cores, invasive margins and immune-cell-rich regions.
In metabolic disease, longitudinal amino acid profiling could potentially identify early metabolic changes before clinical disease becomes apparent.
The combination of metabolomics and clinical phenotyping may ultimately support individualized amino acid-based interventions.

26. CONCLUSION
Amino acids are no longer viewed simply as substrates for protein synthesis. They constitute an interconnected metabolic network that integrates nutrition, energy metabolism, nitrogen homeostasis, redox regulation, cellular signaling and immune function.
The emerging evidence demonstrates that amino acid metabolism is strongly associated with cancer, diabetes, cardiovascular disease and kidney disease. In cancer, amino acid metabolic reprogramming supports proliferation, biosynthesis, redox balance and immune evasion, while also creating metabolic vulnerabilities that may be therapeutically exploited. In cardiometabolic disease, altered BCAA and other amino acid pathways may provide important mechanistic and biomarker information, although causal relationships remain complex. The kidney is a major regulator of amino acid homeostasis, and renal disease can produce profound alterations in amino acid metabolism.
The future of amino acid research therefore lies in moving from descriptive measurement toward mechanistic understanding. Integration of metabolomics, stable-isotope tracing, molecular biology and precision nutrition may provide new opportunities for disease prediction and targeted intervention.
Ultimately, amino acid metabolism represents a promising interface between biochemistry, nutrition, systems biology and clinical medicine. Continued investigation of tissue-specific metabolic networks and patient-specific metabolic phenotypes will be essential for translating these findings into safe and effective therapeutic strategies.

REFERENCES
1. Ling ZN, Jiang YF, Ru JN, et al. Amino acid metabolism in health and disease. Signal Transduction and Targeted Therapy. 2023;8:345. doi:10.1038/s41392-023-01569-3.
2. Knol MGE, Wulfmeyer VC, Müller RU, Rinschen MM. Amino acid metabolism in kidney health and disease. Nature Reviews Nephrology. 2024;20:771–788. doi:10.1038/s41581-024-00872-8.
3. Chen J, Cui L, Lu S, Xu S. Amino acid metabolism in tumor biology and therapy. Cell Death & Disease. 2024;15:42. doi:10.1038/s41419-024-06435-w.
4. McGarrah RW, White PJ. Branched-chain amino acids in cardiovascular disease. Nature Reviews Cardiology. 2023;20:77–89. doi:10.1038/s41569-022-00760-3.
5. Ishii I, Bhatia M. Amino Acids in Health and Disease: The Good, the Bad, and the Ugly. International Journal of Molecular Sciences. 2023;24:4931. doi:10.3390/ijms24054931.

6. Moreno-Vedia J, Llop D, Rodríguez-Calvo R, et al. Serum branched-chain amino acids are increased in type 2 diabetes and associated with atherosclerotic cardiovascular disease. Cardiovascular Diabetology. 2023;22:249. doi:10.1186/s12933-023-01958-6.
7. Amino acid metabolism and atherosclerotic cardiovascular disease. 2024 review.
8. Liu X, Ren B, Ren J, et al. The significant role of amino acid metabolic reprogramming in cancer. Cell Communication and Signaling. 2024;22:380.
9. Amino acid metabolic reprogramming in the tumor microenvironment and its implication for cancer therapy. Journal of Cellular Physiology. 2024. doi:10.1002/jcp.31349.
10. Amino acids in cancer: Understanding metabolic plasticity and divergence for better therapeutic approaches. Cell Reports. 2025;44:115529. doi:10.1016/j.celrep.2025.115529.
11. Ge M, Xu Y, Cui L, et al. Targeting amino acid in tumor therapy. Frontiers in Oncology. 2025;15. doi:10.3389/fonc.2025.1582116.
12. Ren S, Zhou X, Wang Z, et al. Amino acids metabolism: a potential target for cancer treatment. Molecular Cancer. 2025;24:307. doi:10.1186/s12943-025-02523-3.
13. Dynamic crosstalk between amino acid metabolism and cancer drug efficacy: From mechanisms to therapeutic opportunities. iScience. 2025;28:112405.
14. Yuan S, Jin LT, Miao Y, Lei QY. The roles of branched-chain amino acids metabolism in tumorigenesis and progression. 2024. doi:10.16288/j.yczz.24-095.
15. Branched chain amino acids harbor distinct and often opposing effects on health and disease. Communications Medicine. 2023;3:172. doi:10.1038/s43856-023-00382-x.
16. Amino acid metabolism in diabetic kidney disease. 2025.
17. Rewiring amino acids in cancer. Biochimica et Biophysica Acta – Reviews on Cancer. 2025. doi:10.1016/j.bbcan.2025.189465.
18. Targeting pivotal amino acids metabolism for treatment of leukemia. Heliyon. 2024. doi:10.1016/j.heliyon.2024.e40;492