AL-FARABI KAZAKH NATIONAL UNIVERSITY
FACULTY OF BIOLOGY AND BIOTECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY



Lecture 7

Biosynthesis of the Nutritionally Nonessential Amino Acids

PhD, Acting Associate Professor, Doktyrbay Gulina

Lecture Plan

1. Nutritional classification and metabolic precursors
2. Nitrogen transfer and the role of glutamate
3. Biosynthesis of individual amino acids
4. Cofactors and integration with central metabolism
5. Physiological significance and clinical examples
6. Student task, conclusion and references

Learning Objectives

Distinguish essential, nonessential and conditionally essential amino acids.

Identify the carbon skeletons and nitrogen donors used in synthesis.

Explain transamination and ATP-dependent amidation.

Outline the synthesis of the 11 amino acids covered in this lecture.

Identify key cofactors and explain precursor dependence.

Relate impaired synthesis to biochemical examples such as PKU.

Nutritional Classification

Category	Meaning	Examples
Essential	Diet must supply them	9: His, Ile, Leu, Lys, Met, Phe, Thr, Trp, Val
Nonessential	Humans can synthesize them	Ala, Asp, Asn, Glu, Ser
Conditionally essential	Synthesis may not meet demand	Arg, Cys, Gln, Gly, Pro, Tyr; context matters

All amino acids have important biological functions. Nutritional classification describes the need for dietary supply.

Carbon Skeletons

Precursor	Main amino acid products
Pyruvate	Alanine
Oxaloacetate	Aspartate, asparagine
Alpha-ketoglutarate	Glutamate, glutamine, proline; arginine via
3-Phosphoglycerate	ornithine
Phenylalanine	Serine, glycine;cysteine carbon skeleton Tyrosine

Cysteine receives sulfur from methionine via homocysteine.

Sources of Nitrogen

Glutamate commonly donates an amino group in transamination.

Glutamine donates its side-chain amide nitrogen in amidation reactions.

Glutamine synthetase incorporates ammonium using ATP.

Carbon metabolism supplies the skeleton. Nitrogen metabolism supplies the amino group.



Carbon skeleton + nitrogen → **Enzyme + cofactor** → **Amino acid**

Transamination

Aminotransferases transfer an amino group between an amino acid and a keto acid.

Pyridoxal phosphate (PLP), derived from vitamin B6, acts as the cofactor.

Most reactions are reversible and release no free ammonium.

Examples: ALT forms alanine from pyruvate. AST forms aspartate from oxaloacetate.

Keto acid + glutamate ⇌ amino acid + alpha-ketoglutarate

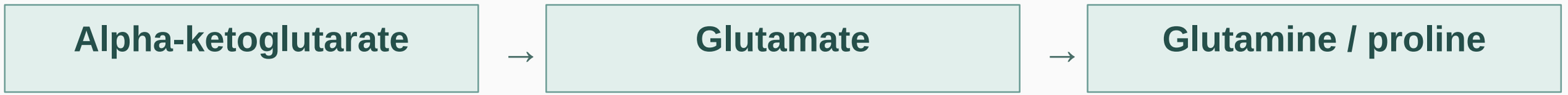
Glutamate: A Nitrogen Hub

Aminotransferases connect glutamate with alpha-ketoglutarate.

Glutamate dehydrogenase also catalyzes reversible reductive amination.

The reaction uses ammonium and NAD(P)H in the synthetic direction.

Glutamate supplies nitrogen for many other amino acids.



Nitrogen incorporation and transfer

Glutamine Biosynthesis

Enzyme: glutamine synthetase.

ATP activates the side-chain carboxyl group of glutamate.

Ammonium incorporation forms the amide group of glutamine.

Glutamine carries nitrogen and donates amide nitrogen for nucleotide and asparagine synthesis.

Glutamate + NH_4^+ + ATP → glutamine + ADP + Pi

Alanine Biosynthesis

Enzyme: alanine aminotransferase (ALT), a PLP-dependent enzyme.

Pyruvate provides the three-carbon skeleton.

Glutamate provides the amino group.

The reversible reaction links amino acid metabolism with glycolysis.

In the glucose-alanine cycle, muscle exports alanine to the liver.

Pyruvate + glutamate ⇌ alanine + alpha-ketoglutarate

Aspartate Biosynthesis

Enzyme: aspartate aminotransferase (AST), using PLP.

Oxaloacetate provides the carbon skeleton.

Glutamate provides the amino group.

Aspartate contributes nitrogen to the urea cycle and to nucleotide synthesis.

Oxaloacetate + glutamate ⇌ aspartate + alpha-ketoglutarate

Asparagine Biosynthesis

Human asparagine synthetase uses aspartate and glutamine.

Glutamine supplies amide nitrogen and becomes glutamate.

ATP activation produces AMP and pyrophosphate (PPi).

The reaction adds an amide group to the side chain of aspartate.

Aspartate + glutamine + ATP + H2O →
asparagine + glutamate + AMP + PPi

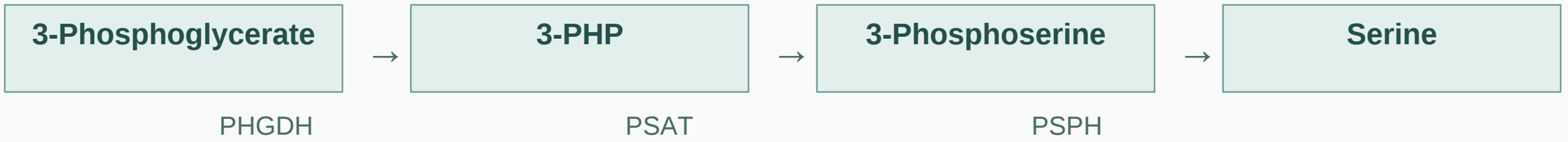
Serine Biosynthesis

The pathway begins with the glycolytic intermediate 3-phosphoglycerate.

PHGDH forms 3-phosphohydroxypyruvate (3-PHP), producing NADH.

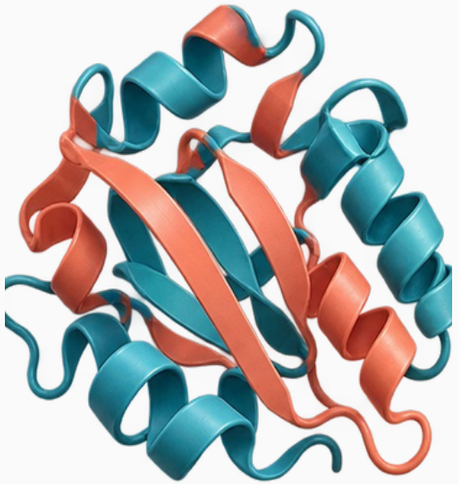
PSAT transfers nitrogen from glutamate using PLP.

PSPH removes phosphate to release serine.



Glycine and One-Carbon Metabolism

Serine hydroxymethyltransferase (SHMT) converts serine to glycine.



The enzyme uses PLP and tetrahydrofolate (THF).

THF receives a one-carbon unit as 5,10-methylene-THF.

This links amino acid synthesis with folate-dependent nucleotide metabolism.

Serine + THF ⇌ glycine + 5,10-methylene-THF + H2O

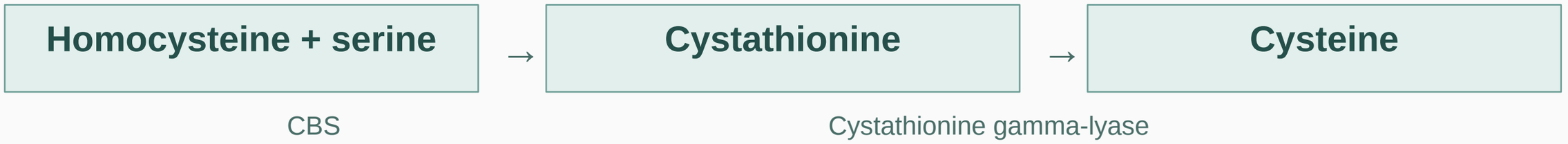
Cysteine: The Transsulfuration Pathway

Serine provides the carbon skeleton. Methionine provides sulfur through homocysteine.

CBS joins homocysteine and serine to form cystathionine.

Cystathionine gamma-lyase releases cysteine. Both enzymes use PLP.

Adequate methionine supply supports cysteine synthesis.



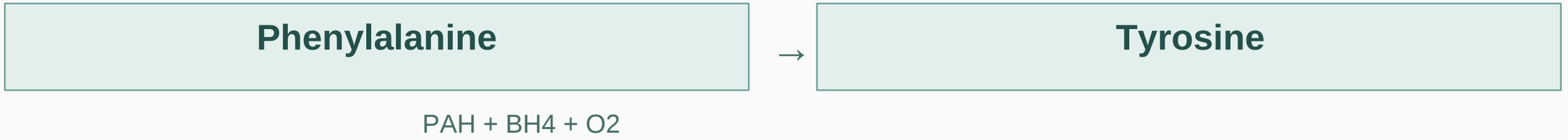
Tyrosine Biosynthesis

Phenylalanine hydroxylase (PAH) converts phenylalanine to tyrosine.

The enzyme requires tetrahydrobiopterin (BH4) and oxygen.

Phenylalanine is nutritionally essential and supplies the complete carbon skeleton.

Tyrosine supports catecholamine, thyroid hormone and melanin synthesis.



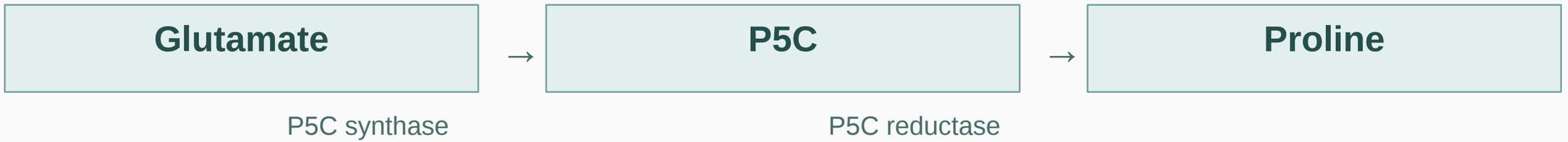
Proline Biosynthesis

Glutamate provides the carbon skeleton.

P5C synthase uses ATP and reducing power to form glutamate semialdehyde.

The semialdehyde cyclizes to pyrroline-5-carboxylate (P5C).

P5C reductase produces proline. Proline is abundant in collagen.



Arginine Biosynthesis

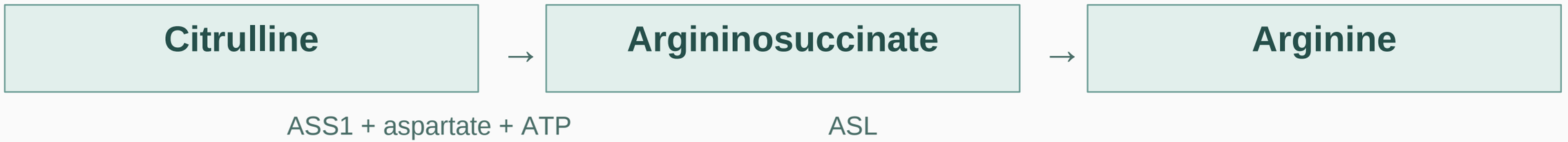
Arginine synthesis involves the intestinal-renal axis and urea-cycle reactions.

The intestine supplies citrulline. The kidney converts citrulline to arginine.

Argininosuccinate synthetase uses aspartate and ATP.

Argininosuccinate lyase releases arginine and fumarate.

Synthetic capacity can be insufficient during growth or metabolic stress.



Key Cofactors

Cofactor	Role	Examples
PLP (vitamin B6)	Amino acid reactions	ALT, AST, PSAT, SHMT, CBS Serine / glycine interconversion
THF (folate)	One-carbon transfer	Phenylalanine hydroxylase Glutamate and proline
BH4	Hydroxylation	synthesis Glutamine and asparagine
NAD(P)H	Reducing power	synthesis
ATP	Substrate activation	

Functions Beyond Protein Synthesis

Amino acid	Selected roles
Glutamate / glutamine	Nitrogen transfer, neurotransmitter cycling, nucleotide synthesis
Serine / glycine	One-carbon metabolism, heme and nucleotide precursors
Cysteine	Disulfide bonds and glutathione
Tyrosine	Catecholamines, thyroid hormones and melanin
Arginine / proline	Nitric oxide precursor / collagen structure

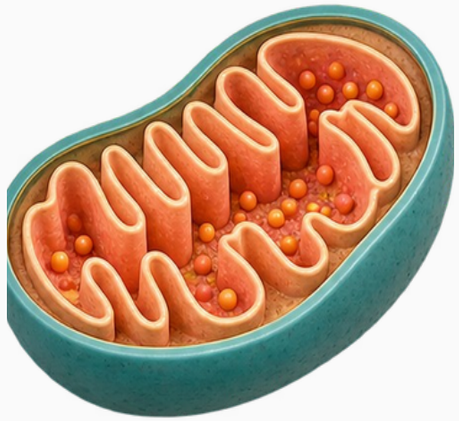
Integration with Central Metabolism

Glycolysis supplies pyruvate and 3-phosphoglycerate.

The citric acid cycle supplies oxaloacetate and alpha-ketoglutarate.

Glutamate distributes amino nitrogen. Glutamine distributes amide nitrogen.

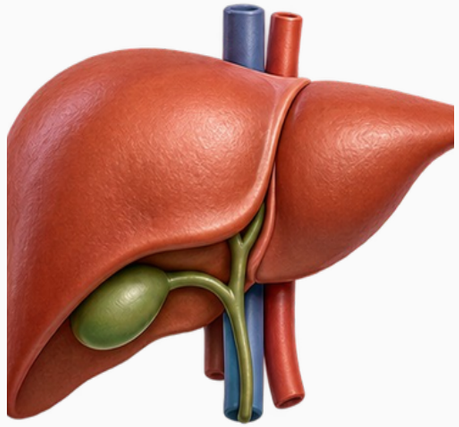
Synthesis depends on precursor supply, energy and enzyme activity.



Different tissues contribute to the whole-body amino acid pool.

Biochemical and Clinical Connections

PAH deficiency restricts phenylalanine-to-tyrosine conversion. Tyrosine becomes nutritionally indispensable in this setting.



CBS deficiency impairs transsulfuration and can lower cysteine availability.

Defects in serine biosynthesis reduce the supply of serine-derived metabolites.

These examples show why endogenous synthesis does not always meet physiological demand.

Task for Students

1. For Ala, Asp, Gln, Ser, Cys and Tyr, tabulate the carbon precursor, nitrogen source, enzyme and cofactor.

2. Explain why ATP is required for glutamine and asparagine synthesis.

3. Trace carbon and sulfur separately during cysteine formation.



4. Explain why impaired PAH activity changes the dietary requirement for tyrosine.

Submit the table and 150–200 words. Cite one textbook.

Conclusion

Human amino acid synthesis connects carbon metabolism with nitrogen transfer.

Glutamate and glutamine act as central nitrogen donors.
Glycolysis and the citric acid cycle provide major carbon skeletons.



PLP, folate and BH4 support distinct biosynthetic reactions.

Dietary precursors and physiological demand determine whether synthesis is sufficient.

References

1. Harper’s Illustrated Biochemistry. 33rd ed. Chapter 27: Biosynthesis of the Nutritionally Nonessential Amino Acids. McGraw Hill / AccessMedicine.

2. Nelson, D. L., Cox, M. M., & Hoskins, A. A. (2021). Lehninger Principles of Biochemistry. 8th ed. Macmillan Learning.

3. Reactome and NCBI PubChem / BioCyc Human Pathways: serine, glycine, glutamate, glutamine and asparagine metabolism.

4. NCBI MeSH: Phenylalanine Hydroxylase, Cystathionine beta-Synthase, Glycine Hydroxymethyltransferase.

5. NCBI GeneReviews: Phenylalanine Hydroxylase Deficiency and Homocystinuria due to CBS Deficiency.

6. MedlinePlus. Amino acids. Nutritional classification. Reviewed 2025.