

Amino Acid Metabolism

Protein Turnover

What is Protein Turnover?

- Protein turnover is the **continuous process** of **synthesizing** new proteins and **degrading** old or damaged ones within cells.
- This is a **dynamic equilibrium**, meaning protein content is not static; it is constantly changing in response to physiological demands.

Why is it important?

- Maintains protein quality by removing damaged or misfolded proteins.
- Provides amino acids for:
 - New protein synthesis
 - Energy production
 - Synthesis of non-protein nitrogenous compounds
- Allows adaptation to changes in cellular needs (e.g., growth, repair, stress, infection)

Key Processes Involved

A. Protein Synthesis

- Occurs on ribosomes via **translation**, using **mRNA templates** transcribed from DNA.
- Requires **all 20 amino acids**, energy (ATP, GTP), tRNAs, ribosomes, and translation factors.

B. Protein Degradation

- Two major systems are involved:

1. Ubiquitin-Proteasome Pathway (in cytosol):

- Targets **short-lived, damaged, or misfolded proteins**.
- Proteins are tagged with **ubiquitin**, a small protein marker.
- Ubiquitin-tagged proteins are directed to the **proteasome**, where they are degraded into **peptides and amino acids**.

2. Lysosomal Pathway (in lysosomes):

- Degrades **extracellular proteins** and **long-lived intracellular proteins**.
- Uses **acid hydrolases** to break proteins into amino acids.

Regulation

- Hormones like **insulin**, **glucocorticoids**, and **thyroid hormones** influence protein turnover.
- **Insulin** promotes synthesis; **glucocorticoids** promote degradation.

- Exercise and nutrient availability also play a role.

Significance:

- Helps in **muscle remodeling, immune response, cell cycle control**, and **adaptation to diet**.
- The **rate of protein turnover** varies by tissue and function:
 - High turnover: intestinal mucosa, liver.
 - Low turnover: muscle, brain.

Nitrogen Balance

Definition:

- Nitrogen balance is the **difference between nitrogen intake and nitrogen loss**.
- It reflects the balance between **protein synthesis and degradation**.
- Since proteins contain about **16% nitrogen**, measuring nitrogen can estimate protein metabolism.

Types of Nitrogen Balance

1. Positive Nitrogen Balance

- **Intake > Loss**
- Indicates **net protein synthesis**
- Occurs in:
 - Growth (children, adolescents)
 - Pregnancy
 - Tissue repair (after injury or surgery)
 - Muscle building

2. Negative Nitrogen Balance

- **Intake < Loss**
- Indicates **net protein breakdown**
- Occurs in:
 - Starvation
 - Severe illness (trauma, burns, infections)
 - Malnutrition
 - Cachexia (wasting)

3. Zero (Neutral) Nitrogen Balance

- **Intake = Loss**
- Seen in healthy adults with no net gain or loss of body protein

Measurement

- **Nitrogen intake** is measured from **dietary protein** (1 gram of protein $\approx$ 0.16 g nitrogen).
- **Nitrogen loss** is measured from:
 - **Urine** (mainly as urea)
 - Feces
 - Sweat, skin, hair, nails

$$\text{Nitrogen Balance} = \text{Nitrogen Intake} - \text{Nitrogen Loss}$$

Clinical Relevance:

- Used to assess **nutritional status**, **response to therapy**, and **renal/liver function**.

Transamination in Amino Acid Metabolism

- Transamination is a reversible biochemical reaction pivotal in amino acid metabolism.
- It facilitates the interconversion of amino acids and the synthesis of non-essential amino acids within the body.
- This process is mediated by enzymes known as transaminases or aminotransferases, which rely on a cofactor, pyridoxal phosphate (PLP)—a vitamin B6 derivative, for activity.
- The essence of transamination lies in transferring an amino group (-NH_2) from an amino acid to an α -keto acid, thereby reshuffling amino groups among amino acids and α -keto acids.

General Reaction



Mechanism of Transamination

1. Amino Group Donation

- An amino acid, referred to as Amino Acid 1, donates its amino group to the PLP cofactor, creating a Schiff base intermediate.

2. Amino Group Transfer

- This amino group is transferred from the Schiff base to an α -keto acid.
- This results in the formation of a new amino acid, termed Amino Acid 2, while transforming the original amino acid into an α -keto acid.

3. Formation of New Compounds

- Consequently, the amino group from Amino Acid 1 is relocated to an α -keto acid, yielding Amino Acid 2, and converting Amino Acid 1 into an α -keto acid.

Significance of Transamination

- Synthesizing non-essential amino acids.
- Facilitating the interconversion of amino acids, which is crucial for metabolic adaptation.
- Producing metabolic intermediates that are utilized in other pathways, such as gluconeogenesis and the citric acid cycle.

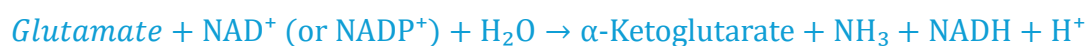
Clinical Relevance

- The activity of transaminases is integral to normal metabolic processes and serves as a biomarker for health conditions.
- Aberrations in transaminase levels can indicate liver damage or specific metabolic disorders, making them important diagnostic markers.

Deamination in Amino Acid Metabolism

- Deamination is an essential biochemical process that facilitates the removal of an amino group (-NH_2) from an amino acid.
- This process yields ammonia (NH_3) and an α -keto acid, playing a pivotal role in the catabolism (breakdown) of amino acids.
- Through deamination, the body can utilize amino acids for energy, produce metabolic intermediates, and manage excess nitrogen effectively.

Reaction



Types of Deamination Reactions

A. Oxidative Deamination

- **Mechanism:** The amino group is removed through an oxidation process, producing an α -keto acid, ammonia, and a reduced cofactor (e.g., NADH).
- **Enzymatic Catalysis:** Dehydrogenases catalyze these reactions. A prominent example is the enzyme glutamate dehydrogenase, which converts glutamate into α -ketoglutarate, generating ammonia and NADH (or NADPH).

B. Non-oxidative Deamination

- **Mechanism:** This involves initially transferring the amino group from the amino acid to a different molecule, typically via a transamination reaction. The amino group is then released as ammonia.
- **Enzymatic Process:** Occurs in a two-step enzymatic process:
 1. A transaminase enzyme transfers the amino group to another molecule.

2. The amino group is released as ammonia, often facilitated by enzymes such as glutamate dehydrogenase. For example, the deamination of alanine to pyruvate involves transferring alanine's amino group to α -ketoglutarate, forming glutamate and pyruvate, followed by the release of ammonia from glutamate.

Ammonia Detoxification

- The ammonia produced during deamination is toxic and must be detoxified.
- The urea cycle, predominantly occurring in the liver, plays a critical role in converting ammonia into urea, a less toxic compound.
- Urea is then safely excreted from the body through the kidneys.

Physiological Significance

- Deamination is integral to amino acid metabolism, enabling the body to adapt to various energy demands and maintain nitrogen balance.
- It allows for the repurposing of amino acids as energy sources and the production of key metabolic intermediates.

Clinical Implications

- Disruptions in deamination processes can lead to elevated ammonia levels, posing significant health risks.
- Such abnormalities can cause metabolic disorders and severe health complications due to ammonia's toxicity.
- Monitoring and managing deamination processes are crucial for preventing these adverse effects and ensuring metabolic health.

Decarboxylation in Amino Acid Metabolism

Decarboxylation

- Decarboxylation is a vital biochemical reaction involving the removal of a carboxyl group (-COOH) from a molecule, releasing carbon dioxide (CO_2).
- In amino acid metabolism, this reaction is essential for converting amino acids into various bioactive compounds, such as amines and neurotransmitters.
- Enzymes called decarboxylases, which often require pyridoxal phosphate (PLP) (a vitamin B6 derivative) as a cofactor, catalyze these reactions.

Key Decarboxylation Reactions in Amino Acid Metabolism

A. Aromatic L-amino acid decarboxylase (AADC)

- **Substrates and Products:** AADC decarboxylates aromatic amino acids like L-dopa and 5-hydroxytryptophan (5-HTP) into dopamine and serotonin, respectively.



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