Tryptophan is an important actor in the NAD de novo pathway.

Tryptophan is primarily involved in the de novo (not salvage) biosynthesis pathway of NAD, serving as the precursor that is metabolized through the kynurenine pathway into quinolinic acid, which is then ultimately converted to NAD+ in the liver and kidney. While the salvage pathway predominantly utilizes dietary niacin derivatives—namely nicotinamide (NAM), nicotinic acid (NA), and nicotinamide riboside (NR)—to restore NAD+ from recycled forms, tryptophan can compensate for NAD+ biosynthesis if the salvage pathway is disrupted or dietary precursors are lacking.[1][2][3][4][5]

Tryptophan's Place in NAD Metabolism

- Tryptophan is converted into NAD+ via the kynurenine pathway, which is most active in the liver and kidney.[3][5][1]
- This de novo pathway is separate from the classical salvage pathway, which recycles NAM, NA, and NR for NAD synthesis.[2][3]
- If the salvage pathway is blocked or dietary niacin is insufficient, tryptophan metabolism can provide a compensatory source of NAD+.[2][3]

NAD Salvage Pathway Overview

- The salvage pathway recycles NAD+ from NAM, NA, and NR rather than using tryptophan directly.[4][3]
- NAMPT (nicotinamide phosphoribosyl transferase) is a key enzyme in this recycling process, converting NAM to NMN, which then forms NAD+.[6][7]
- Most tissues rely on the salvage pathway for maintaining NAD+ pools, while de novo synthesis via tryptophan is predominantly hepatic and renal.[5][2]

Compensation Mechanism

- When NAD+ precursors (NAM, NA, NR) are not adequately available from diet or salvage, de novo conversion from tryptophan becomes critical to prevent deficiencies such as pellagra.[3][5]

- This compensation ensures systemic NAD+ homeostasis in conditions where the salvage pathway is compromised.[2][3]

In summary, tryptophan is a major contributor to de novo NAD+ synthesis rather than direct involvement in the salvage pathway, but its metabolic flexibility allows the maintenance of NAD+ levels when salvage recycling is impaired or dietary niacin is low.[5][3][2]

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