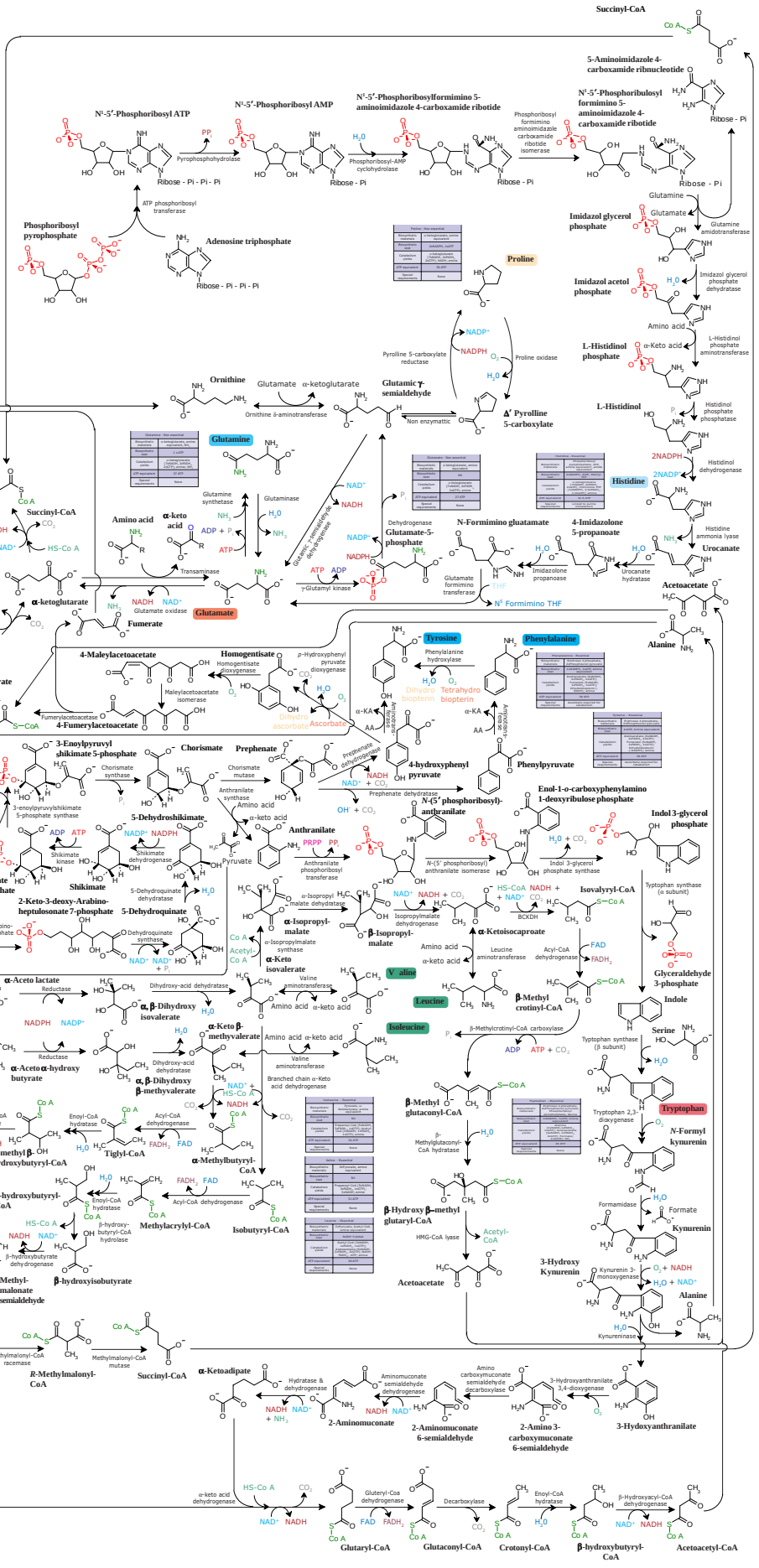
Amino Acid Metabolism: Biosynthesis and Catabolism of the Twenty Standard Amino Acids

The biosynthesis and degradation of the twenty standard amino acids represent the complexity and ingenuity of metabolism at its most astounding. The carbons skeletons of all of these disparate and diverse compounds are derived, universally throughout life on this planet, from glycolytic intermediates, metabolites of the Krebs cycle and the Pentose phosphate pathway, and in the case of histidine from nucleotide (purine) metabolism. Many amino acids that are superficially unrelated have similar sources: aspartate, asparagine, lysine, threonine and methionine all have their origin in the Krebs cycle metabolite oxaloacetate for example. And yet one immediate and striking factor becomes apparent once the detail and complexity of these pathways is assimilated: the similarity apparently unconnected pathways have to each other, and to the other pathways of carbohydrate or lipid metabolism, varient in such a subtle and continuous manner to supply a continuous range of organic functional groups with which to array the amino acids used in protein synthesis. Thus, the two acidic amino acids glutamate and aspartate are both derived from simple transaminations of two anaologous (even homologous) metabolites of the Krebs cycle, α-ketoglutarate and oxaloacetate. Amidisation gives two polar amino acids, glutamine and asparagine, and further derivatives are produced by NADPH dependent reduction of the terminal carboxyl group to a aldehyde, leading to cyclc schiff bases, and ultimately metabolised to lysine and proline respectively. Pleasing, and diagramatically prophitable, as this symettry is, it is nothing as compared to the interlocking and cointually shifting motifes of β-oxidation and claisen ester condensation, Krebs cycle reactions and continually recurring reaction such as the decarboxylation of α-keto acids to yield acyl-CoA, and the almost mathematically propitious importance of odd and even number carbon chains. Pathways such as the formation of the brached chain hydrophobic amino acids (leucine, isoleucine and valine) are a direct example of this: formation of the principles, isoleucine and valine, occurs through the mixed claisen/aldol condensation of acetyl-CoA, as directly derived from pyruvate, with either pyruvate itself or its four carbon homologue, α-ketobutyrate; itself derived from threonine in a reaction primarily attributed to its fellow hydroxy-bearing amino acid in serine dehydratase; in direct analogy with the first reaction of the Krebs cycle. The adducts are then reduced and dehydrated, immediately reminiscent of the stages following ester condensation in fatty-acid biosynthesis. This combination is repeated upon itself in the conversion of the metabolites to leucine; a futher condensation with acetyl-CoA ; but in contrast, the adduct is isomerised and oxidatavley decarboxylated in a manner very similar to the continuing steps in the Krebs cycle. All the ingenuity of the basic metabolic pathways of carbohydrates and fatty acids has been harnessed to yield a spectrum of protein components; common motifs are mixed and recombined, defined chemistry is applied to novel substartes, and echoes of each pathway reverberate throughout the whole system. Amino acid biosynthesis is not only a symbol for the complexity and elegance of metabolism; it also represents the ever recombining genome, the functional exon as the unit of recombination in eukaryotes and the subtlety of nature in expanding a handful of effective chemical mechanisms throught the entirely logical, but profoundly mysterious methods of natural selection.

Catabolism of each amino acid is at least as fascinating, and offers some insight into the metabolic "value" of each amino acid: the amount of ATP or reducing power that can be obtained through complete oxidation of its carbon chain to CO_2 and water. In addition, since mammals ingest every standard amino acid in the form of protein, but rarely use all of this for protein synthesis, catabolic pathways for every one must exist throughout the whole animal kingdom. Again, the auspices of the enzymes derived from standard metabolism are more than in evidence. Amino acids are catabolised either to glucogenic (α-ketoglutarate, oxaloacetate, fumerate, succinyl-CoA, or pyruvate) or ketogenic (acetyl-CoA, acetoacetate) products, much depending on the oxdisation state of the amino acid: phenylalanine, for instance, is both; the highly reduced phenyl group becoming (after consideable aerobic oxidation) HMG-CoA, and the peptide moiety becoming fumerate.

The metabolism of the amino acids is in itself another basis for more complex or specialised reactions, utilising the scemata of these pathways in the same way that the reactions characterised below employ the other metabolic pathways. Common enzyme structure, mechanism and themes can be detected throughout pathways in disparate organisms, in different kingdoms, in entirely different environments. The universality of the basic reactions (as well as the informative exceptions) is yet another example of the deep rooted, and all pervading, unity of the life on this planet.



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