Degradation of amino acid carbon skeletons

About twenty amino acids are incorporated into human proteins (there are 22 of them including selenocysteine and pyrrolysine). Amino acids that are not used in metabolism for any reason, e.g. after they have been released from proteins, are not excreted as a whole, but are catabolized into smaller fragments. At the beginning of the degradation, the amino group is usually split off. Then the remaining carbon skeleton is broken down. The pathways through which this happens are variously complex. Here we will show the common mechanisms and give some examples.

The breakdown of the carbon skeleton of all amino acids ends in one of these seven substances:

1. pyruvate,
2. acetyl-CoA,
3. acetoacetyl-CoA,
4. α-ketoglutarate,
5. succinyl-CoA,
6. fumarate,
7. oxalacetate.

These products then enter the energy metabolism. They can either be further oxidized to carbon dioxide and water in the Krebs cycle, or they can be converted to other fuels. Some can produce **glucose** , others only **ketone bodies** and **fatty acids** . Accordingly, we distinguish between so-called **glucogenic** and **ketogenic** amino acids.

Ketogenic **amino acids** include those that lead to the formation of **acetyl-CoA** and **acetoacetyl-CoA** – leucine and lysine (beginning with the letter L). Glucogenic **amino acids** include those that lead to the formation of the remaining five products - **pyruvate** , **α-ketoglutarate** , **succ-CoA** , **fumarate** or **oxaloacetate** - serine, threonine, cysteine, methionine, aspartate, glutamate, asparagine, glutamine, glycine, alanine, valine, proline, histidine and arginine.

There are also amino acids with two degradation products – one of them is glucogenic and the other is ketogenic. We call them keto and glucogenic amino acids – they include isoleucine, phenylalanine, tyrosine a tryptophan.

The following overview shows which amino acids are degraded into which products:

1) **Acetyl-CoA** and **acetoacetyl-CoA**

purely ketogenic are Lys and Leu, several other amino acids provide degradation products both glucogenic and ketogenic – Phe, Tyr, Trp, Ile;

2) **α-ketoglutarate**

Five-carbon – Glu, Gln, Pro, Arg and His;

3) **Suc-CoA**

non-polar amino acids – Met, Ile a Val;

4) **Fumarate**

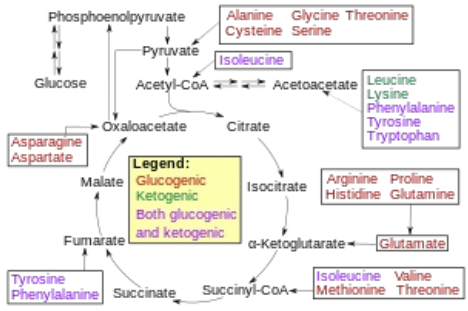
Phe, Tyr;

5) **Oxalacetate**

four-carbon amino acids – Asp a Asn;

6) **Pyruvate**

Cys, Ala, Ser, Gly, Thr, Trp.



Catabolism of essential amino acids

Degradation of **branched-chain amino acids** – Val, Leu and Ile

It is characteristic of these amino acids that they are **degraded** not in liver cells, but mainly in **extrahepatic tissues** – high activity especially in muscle cells. These contain a specific transaminase producing the respective α-keto acids – the so-called **keto analogues of branched amino acids** . This transaminase is absent in liver cells. Keto analogs are converted to **acyl-CoA derivatives** by the action of **a dehydrogenation complex** , which catalyzes oxidative decarboxylation and dehydrogenation.

A genetic defect of this dehydrogenation complex causes a disease called **maple syrup urine disease** . In this relatively rare disease, the corresponding α-ketoacids accumulate in the tissues and body fluids (they cause the characteristic smell of maple syrup - burnt sugar in the urine). The defect causes abnormal brain development, mental retardation and can even result in the death of the individual.