MAPLE SYRUP URINE DISEASE

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Ahornsirupkrankheit

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Content

- General
- Symptoms
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general

- autosomal-recessive
- disturbance in the amino acid metabolism

  → high concentration of branched-chain amino acids and their toxic by-products in blood and urine

  → lead to a sweet-smelling urine

Symptoms

- mental and physical retardation
- feeding problems, vomiting, dehydration
- lethargy, hypotonia
- seizures
- coma
- brain damage → death

Diagnosis

- detection of a defect of the enzyme in amnion cells (prenatal)
- newborn screening by mass spectrometric processes in plasma und urine (first 3 days)
- 2,4-Dinitrophenylhydrazin (DNPH) in the urine → positive if the urine gets red
- test of the breath with labeled ^{13}C-isotope

Clinical subtypes

- Classic Severe MSUD
- Intermediate MSUD
- Intermittent MSUD
- Thiamine-responsive MSUD
- E3-Deficient MSUD with Lactic Acidosis

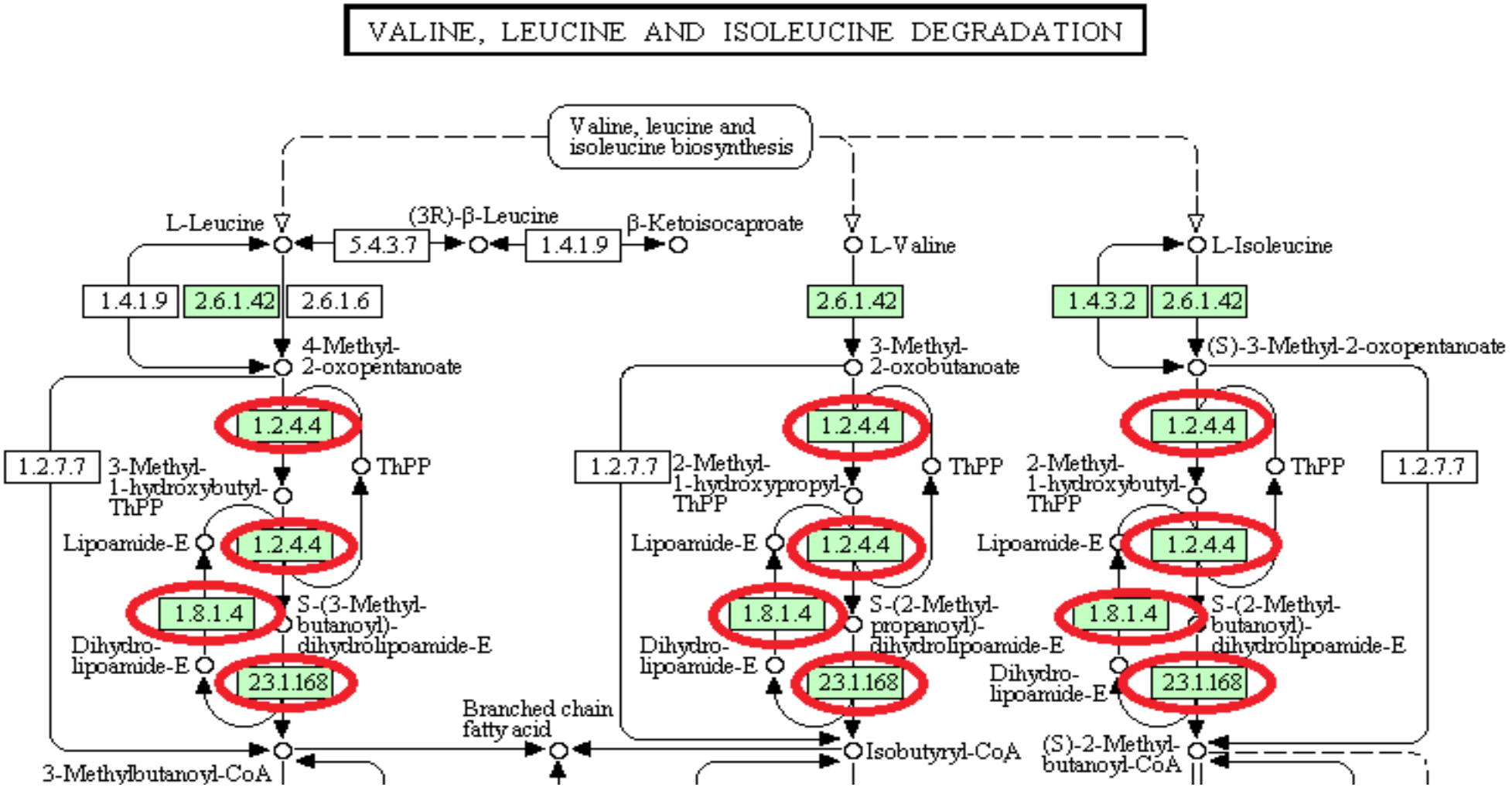
Protein

- MSUD is caused by mutations in the following genes:
  - BCKDHA (Branched-Chain Keto Acid Dehydrogenase E1, α-subunit)
  - BCKDHB (E1, β-subunit)
  - DBT (Dihydrolipoamide Branched-Chain Transacylase, E2)
  - DLD (Dihydrolipoamide Dehydrogenase, E3)

BCKD-Complex

- Those 4 gene products form a complex: the branched-chain alpha-keto acid dehydrogenase complex (BCKD)
- breakdown of leucine, isoleucine and valine
- L, I and V are particularly part of protein-rich food like meat, eggs and milk

Pathway


VALINE, LEUCINE AND ISOLEUCINE DEGRADATION
Valine, leucine and isoleucine biosynthesis
L-Leucine
(3R)-β-Leucine
β-Ketoisocaproate
5.4.3.7
1.4.1.9
1.4.1.9
2.6.1.42
2.6.1.6
4-Methyl-2-oxopentanoate
1.2.4.4
1.2.7.7
3-Methyl-1-hydroxybutyl-ThPP
ThPP
Lipoamide-E
1.2.4.4
1.8.1.4
S-(3-Methyl-butanoyl)-dihydrolipoamide-E
Dihydro-lipoamide-E
23.1.168
3-Methylbutanoyl-CoA
L-Valine
2.6.1.42
3-Methyl-2-oxobutanoate
1.2.4.4
1.2.7.7
2-Methyl-1-hydroxypropyl-ThPP
ThPP
Lipoamide-E
1.2.4.4
1.8.1.4
S-(2-Methyl-propanoyl)-dihydrolipoamide-E
Dihydro-lipoamide-E
23.1.168
Branched chain fatty acid
Isobutyryl-CoA
L-Isoleucine
1.4.3.2
2.6.1.42
(S)-3-Methyl-2-oxopentanoate
1.2.4.4
2-Methyl-1-hydroxybutyl-ThPP
ThPP
1.2.7.7
Lipoamide-E
1.2.4.4
1.8.1.4
S-(2-Methyl-butanoyl)-dihydrolipoamide-E
Dihydro-lipoamide-E
23.1.168
(S)-2-Methyl-butanoyl-CoA

Causes

- Subtypes 1-4 are caused by mutations in any of these genes:
  - BCKDHA, BCKDHB, DBT, DLD
- Subtype 5 is only caused by a mutation in the
  - E3 gene

Sources

- http://www.ncbi.nlm.nih.gov/omim/248600
- http://en.wikipedia.org/wiki/Maple_syrup_urine_disease
- http://www.genome.jp/kegg-bin/show_pathway?hsa00280