

Phenylketonuria, also known as phenylalanine hydroxylase deficiency, is a recessively inherited disease caused by a variation in the phenylalanine hydroxylase (PAH) gene, which affects the production of the enzyme of the same name, which is needed to break down the amino acid phenylalanine. Untreated phenylketonuria in newborns will lead to a series of symptoms within a few months, such as impacted mental and physical development and skin pigmentation, as well as epilepsy, eczema, and a specific odor to the skin or urine, induced by the excess of phenylalanine in the body. As the symptoms are early-onset and life-impacting to -threatening, screening for phenylketonuria is often one of the first diagnostics performed after birth. If the disease is found, treatment is performed using a phenylalanine-limiting diet, for example strongly reducing the intake of protein. While not curable, if treatment begins early humans with phenylketonuria can live a “normal” life, barring the dietary restrictions.

Sources:

<https://www.omim.org/entry/261600?search=phenylketonuria&highlight=phenylketonuria> (20.06.2022),

<https://www.mayoclinic.org/diseases-conditions/phenylketonuria/symptoms-causes/syc-20376302> (20.06.2022)

> Human (Homo sapiens)

>sp|P00439|PH4H_HUMAN Phenylalanine-4-hydroxylase OS=Homo sapiens
OX=9606 GN=PAH PE=1 SV=1

MSTAVLENPGLGRKLSDFGQETSYIEDNCNQNGAISLIFSLKEEVGALAKVLRRLFEEENDVNLTHIE
SRPSRLKKDEYEFFTHLDRSLPALTNIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFA
NQILSYGAELDADHPGFKDPVYRARRKQFADIAYNYRHGQPIPRVEYMEEEKKTWGTVFCTLKSLY
KTHACYEYNHIFPLLEKYCGFHEDNIPQLEDVVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFH
CTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIIYWFTVE
FGLCKQGDSIKAYGAGLLSSFGEQYCLSEKPKLLPLELEKTAIQNYTVTEFQPLYYVAESFNDAK
EKVRNFAATIPRPFVRYDPYTQRIEVLDTQQLKILADSINSEIGILCSALQKIK

> Chimpanzee (Pan troglodytes)

>XP_001156919.1 phenylalanine-4-hydroxylase [Pan troglodytes]

MSTAVLENPGLGRKLSDFGQETSYIEDNCNQNGAISLIFSLKEEVGALAKVLRRLFEEENDINLTHIE
SRPSRLKKDEYEFFTHLDRSLPALTNIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFA
NQILSYGAELDADHPGFKDPVYRARRKQFADIAYNYRHGQPIPRVEYMEEEKKTWGTVFCTLKSLY
KTHACYEYNHIFPLLEKYCGFHEDNIPQLEDVVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFH
CTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIIYWFTVE
FGLCKQGDSIKAYGAGLLSSFGEQYCLSEKPKLLPLELEKTAIQNYTVTEFQPLYYVAESFNDAK
EKVRNFAATIPRPFVRYDPYTQRIEVLDTQQLKILADSINSEIGILCSALQKIK

> Gorilla (Gorilla gorilla)

>XP_004053827.1 phenylalanine-4-hydroxylase [Gorilla gorilla
gorilla]

MSTAVLENPGLGRKLSDFEQETSYIEDNCNQNGAISLIFSLKEEVGALAKVLRRLFEEENDINLTHIE
SRPSRLKKDEYEFFTHLDRSLPALTNIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFA
NQILSYGAELDADHPGFKDPVYRARRKQFADIAYNYRHGQPIPRVEYMEEEKKTWGTVFCTLKSLY
KTHACYEYNHIFPLLEKYCGFHEDNIPQLEDVVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFH
CTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIIYWFTVE

FGLCKQGDSIKAYGAGLLSSFGEQYCLSEKPKLLPLELEKTAIQNYTVTEFQPLYYVAESFNDAK
EKVRNFAATIPRPFVRYDPYTQRIEVLNNTQQKILADSINSEIGILCSALQKIK

> Tufted capuchin (*Sapajus apella*)

>XP_032155339.1 phenylalanine-4-hydroxylase isoform X1 [*Sapajus apella*]

MSTAVLENRGLGRKLSDFGQETSYIEENATQNGAISLIFSLKEEVGALAKVLRLFEENDINLTHIE
SRPSRLKKDEYEFFTLDKRSPLALANIIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFA
NQILSYGAELDADHPGFKDPVYRARRKQFADIAYNYRHGQPIPRVEYTEEEKKTWGTVFRTLKSLY
KTHACYEYNHIFPLLEKYCGFHEDNIPQLEDVVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFH
CTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIIYWFTVE
FGLCKQGDIAKAYGAGLLSSFGEQYCLSDKPTLLPLELEKTAIQKYTVTEFQPLYYVAESFNDAK
EKVRNFAATIPRPFVHYDPYTQRIEVLNNTQQKILADSINSEIGILCSALQKIK

> Arabian camel (*Camelus dromedarius*)

>XP_010988325.2 phenylalanine-4-hydroxylase [*Camelus dromedarius*]

MHSLGASMSAAVLENGGFSRKFSDFGQETSYIEDNANQNGTISLIFSLKEEVGALAKVLRLFEEND
INLTHIESRPSRLKKDEYEFTYLDKHSVPALANIIKILRHDIGATVHELSDRDKKDTVPWFPRTI
QELDRFANQILSYGEELDADHPGFKDPVYRARRKQFADIAYNYRHGEPIPRVEYMEEEKKTWGTVF
RTLKSLYKTHACYEHNHIFPLLEKYCGFHEDNIPQLEDVVSQFLQTCTGFRLRPVAGLLSSRDFLG
LAFRVFHCCTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDDYVEKLAT
IIYWFTVEFGLCKQGDSIKAYGAGLLSSFGEQYCLSGKPELLPLELEKTAVQKYTVTEFQPLYYVA
ESFNDAKEKVRNFAATIPRPFVRYDPYTQRIEVLNNTQQKILADSINSEVIGILCSALQKIK

> Alpaca (*Lama pacos* / *Vicugna pacos*)

>XP_006205956.1 phenylalanine-4-hydroxylase [*Vicugna pacos*]

MSAAVLENGGFSRKFSDFGQETSYIEDNTNQNGTISLIFSLKEEVGALAKVLRLFEENDINLTHIE
SRPSRLKKDEYEFTYLDKRSVPALANIIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDKFA
NQILSYGAELDADHPGFKDPVYRARRKQFADIAYNYRHGEPIPRVEYTEEEKKTWGTVFRTLKSLY
KTHACYEHNHIFPLLEKYCGFHEDNIPQLEDVVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFH
CTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDDYVEKLATIIYWFTVE
FGLCKQGDSIKAYGAGLLSSFGEQYCLSGKPELLPLELEKTAVQKYTVTEFQPLYYVAESFNDAK
EKVRNFAATIPRPFVRYDPYTQRIEVLNNTQQKILADSINSEVIGILCSALQKIK

> Horse (*Equus ferus caballus*)

>XP_001497778.1 phenylalanine-4-hydroxylase [*Equus caballus*]

MSAVVLENRGFGRKFSDFGQETSYIEDNSNPNGAISLIFSLKEEVGALAKVLRLFEENDINLTHIE
SRPSRLKKDEYEFTYLDKRSMPLANIIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFA
NQILSYGAELDADHPGFKDPVYRARRKYFADIAYNYQHGGQPIPRVEYTEEEKKTWGTVFRTLKSLY
KTHACYEHNHIFPLLEKYCGFREDNIPQLEEVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFH
CTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIIYWFTVE
FGLCKQGDSIKAYGAGLLSSFGEQYCLSDKPKLLPLDLEKTAVQEYTITEFQPLYYVAESFNDAK
EKVRNFAATIPRPFVRYDPYTQRIEVLNNTQQKILADSINSEVIGILCSALQKIK

> Canada lynx (*Lynx canadensis*)

>XP_030179385.1 phenylalanine-4-hydroxylase [*Lynx canadensis*]

MSAVVLENRGFGRKLSGQETSYIEDNSNQDGAISLIFSLKEEVGALAKVLRLFEENDINLTHIES
RPSRLKKDEYEFTYLDKRSMPLANIIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFAN
QILSYGAELDADHPGFKDPVYRARRKQFADIAYSRYHGGQPIPRVEYTEEEKKTWGTVFRTLKSLYK

THACYEHNHIFPLLEKYCGFREDNIPQLEEVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFHC
TQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIWFTVEF
GLCKQGDSIKAYGAGLLSSFGEQYCLSGEPKLLPLELEKTAVQEYTVTEFQPLYYYVAESFNDAKE
KVRNFAATIPRPFSVRYDPYTQRIEVLNDNTQQLKILADSINSEVGILCNALQKIK

> Domestic cat (*Felis catus*)

>XP_019690977.1 phenylalanine-4-hydroxylase [*Felis catus*]

MSAVVLENRGFGRKLSGQETSIEDNSSQDGAISLIFSLKEEVGALAKVLRRLFEEENAINLTHIES
RPSRLKKDEYEFFTYLDKRSMPLVLANIIKILRHDIGATVHELSDRDKKDTVPWFPRTIQELDRFAN
QILSYGAELDADHPGFKDPVYRARRKQFADIAYSYRHGQPIPRVEYTEEEKKTWGTVFRTLKSLYK
THACYEHNHIFPLLEKYCGFREDNIPQLEEVSQFLQTCTGFRLRPVAGLLSSRDFLGGLAFRVFHC
TQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFAQFSQEIGLASLGAPDEYIEKLATIWFTVEF
GLCKQGDSIKAYGAGLLSSFGEQYCLSGEPKLLPLELEKTAVQEYTVTEFQPLYYYVAESFNDAKE
KVRNFAATIPRPFSVRYDPYTQRIEVLNDNTQQLKILADSINSEVGILCSALQKIK

Guide tree:

(1, 2)
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(1+2+3, 4, 5, 6, 7, 8, 9)
(5, 6)
(1+2+3, 4, 5+6, 7, 8, 9)
(8, 9)
(1+2+3, 4, 5+6, 7, 8+9)
(4, 1+2+3)
(1+2+3+4, 5+6, 7, 8+9)
(7, 8+9)
(1+2+3+4, 5+6, 7+8+9)
(5+6, 1+2+3+4)
(1+2+3+4+5+6, 7+8+9)