Lec. 3 / Dr. Diala

last 2 slides of **slide 1 :**

- if we have a deficiency in any of the enzymes of urea cycle , we'd have it impaired resulting in accumulation of ammonia and increase its conc. in the blood that's mainly affects the CNS.

-acquired hyperammonemia is due to destruction of hepatocytes.

-congenital hyperammonemia usually follows AR (autosomal recessive) inheritance pattern, except OTC deficiency which is x-linked and more predominant in males.

- an example of synthetic compounds that bind covalently to AAs is phenylacetate that binds to glutamine .

Slide 2 :

Slide 1 +2 :

We except different pathways to the left molecules of AAs after removing the nitrogen part because we have different R-chains, and depending on the final product of the catabolism process AAs are categorized into 3 groups: glucogenic , ketogenic and both .

Ketogenic AAs are Leucine and Lysine .

Both : produces different types of compounds with several pathways to degrade or to be metabolized . (the aromatic AAs :{ Tyr , Trp , Phe} and ILe)

As we have 7 intermediates we can catatgorize the AAs into 7 groups depending on the end products of their metabolisim .

Slide 3 : **AAs that produce OXALOACETATE : Asn and Asp** (Asn is deaminated to Asp which is transaminated to oxaloacetate)

Slide 4 **: AAs that form α-ketoglutarate via glutamate** which can be deamintaed to an alpha-keto acid . (**glutamine-Gln- , Pro , Arg , His)**
- Pro is converted to Glu by opening the cycle-structure.

Slide 5 :

-**His has an imidazole group** in its R-chain that makes it really different from Glu , so it has to be converted and modified to a similar structure . First step deals with the amino group only to produce Urocanic acid that go through multiple steps to open the ring and break the double bond resulting in a molecule called **FIGlu which is very close to Glu** (this step is mediated by tetrahydrofolate –active form of B9)

slide 6: none

slide 7:

Amino acids that form pyruvate : Ala , Ser, Gly , Cys , Thr
-Gly has two metabolic pathways :

a) oxidation : that ends up with CO_2 and NH_3
b) conversion to serine which is deaminated with removal of H_2O to produce pyruvate.

Slide 8 :

Cysteine has a very close structure to serine (there is a sulfur group instead of hydroxyl group)

cystine is reduced to cysteine in oxidation rxn by oxidation of NADH to NAD+

threonine has an OH-group on the middle carbon

slide 9 :

Amino acids that form fumarate : **Phe, Tyr**

-Phe hydroxylase adds hydroxyl group to produce tyrosin , so Phe is an essential AA

Slide 10 :

Amino acids that form succinyl CoA (a TCA cycle intermediate and glucogenic compound) : **Val, Ile, Thr,Met**

-Valine and isoleucine are branched-chain amino acids. Remember that in alpha-helix there are factors that constrict the formation of the helix as the presence of 2 branched-chain AAs next to each other that branch quickly and take more space leads to what is called steric hindrance.

Slide 11 :

Met :has a sulfur atom in between 2 carbons , it is a non-polar essential AA used in protein synthesis as a first AA. It can be used for production of other AAs that contain sulfur as cysteine(non-essential).

-SAM : methyl carrier (donor) , is used for synthesis of many compounds or modifications of nucleic acids specifically the methylation of DNA. (methylation turns off genes)
slide 12:

Homocysteine has 2 pathways :

a) in presence of B12 and methyl-tetrahydrofolate is converted to Met and tetrahydrofolate.

b) in presence of B6 is converted to cysteine

slide 13:none

slide 14:

Amino acids that form acetyl CoA or acetoacetyl CoA : **Leu, Ile, Lys, Trp .Note: {Phe and Tyr produce acetoacetate}**

slide 15:

Catabolism of the branched-chain amino acids Ile, Leu, Val

-these AAs are metabolized to alpha-keto acids that are further metabolized to derivatives of A-CoA and acetoacetyl CoA to produce ketone bodies.

Notes related to folic acid(folate) discussed through all the lecture :

-folic acid(B9) : need to be activated after ingestion with food into tetrahydrofolate(THF) and even tetrahydrofolate can be activated into other forms to contribute the reactions .

-folic acid increases the fertility so women take it if they are planning to get pregnants before 2 months .Furthermore, pregnants need it to reduce the risk of neural tube defects in the fetus .

-around 25% of Jordanian people have a mutation in the gene that codes the enzyme that converts the folic acid into its active form , so that active form is added to food as supplements to avoid accumulation of the inactive form which may contributes to other diseases.

-found especially in dark green leafy vegetables .

- THF can carry the carbon in many forms :

a)carbon atom as formyl(H-c=O) , for purine synthesis

b)methenyl(CH) , the carbon connected to the structure by 2 bonds (single and double), for synthesis of other molecules.

c)methylene(CH2) , the carbon is connected via 2 single bonds , for synthesis of some derivatives od nucleic acids

d) CH3 (methyl) , for methionine degradation pathway.

Done by : Abdullah Sulaiman

Best wishes ☺