Lec. 2 / Dr. Diala

slide 1 :

-The product of the stomach still has some peptide bods, but almost full digestion will be due to this combination of enzymes that ends up with hydrolyzing peptide bonds between different AAs.

-At the picture you notice the sequence after or before which each of these peptidases can act or cut.(Don't memorize the AAs)

*serine endopeptidases : (cuts after)

- trypsin : cuts after the basic AAs (Arg, Lys)
-chymotrypsin: cuts after the aromatic AAs (Trp,Tyr,Phe) , Met and Leu
- Elastase :cuts after (Ala, Gly, Ser)

*exopeptidases : (cuts before)

-carboxypeptidase A : cuts before the hydrophobic AAs (Ala, Ile,Leu,Val)
- carboxypeptidase B: cuts before the basic AAs (Arg, Lys)

-Cleavege of AA by endopeptidase takes place where charged group ends up at the C-terminal.

Slide2:

- in addition to the pancreatic enzymes , we have an enzyme called **aminopeptidase** which is a local intestinal peptidase produced in the small intestinal cells. It **finalizes the whole process of digestion.**

Slide3:

- now we have free AAs or di- and tri- peptides will be absorbed and loaded to the portal circulation as a checkpoint for detoxification of some AAs , metabolism and distribution of some to cells via systemic(general) circulation.

-absorption process takes place by different mechanisms :

a- Na+-linked secondary transport system: for free AAs at the apical surface through microvilli.
b- H+-linked transport system : for di- and tri- peptides

slide 4:

-Celiac disease : (حساسية القمح) , patients with this disease suffer from deficiency of anything is absorbed by small intestinal cells as V B12 or folic acid (V B9)

- deficiency in pancreatic enzymes as peptidases (proteases) and lipases leads to less digestion .
- Steatorrhea : high amounts of lipids in the stool.

Slide 5 :

-absorption is done by small intestine while reabsorption by the proximal tubule of the kidney.

-cysteine is not for proteins synthesis only , but also for peptides as GSH , Vasopressin .. etc.

- cystine is a dimer of cysteine connected by disulfide bridges , it is converted to cysteine then transported by the COAL system.

-Ornithine is present in our body but not in proteins as there's no codon carried by tRNA for it . (Non-protein AA)

Slide6 :

-Cystinuria :a defect in the transport(reabsorption) of cystine results in accumulation , secretion through urine and precipitation to form kidney stones.(In COAL system specificly)
- Oral hydration (more fluids) is the treatment as it improves the function of the kidney.

slide 7:
now we have free AAs leave to liver for metabolism and can be distributed to different types of cells through the circulation.

- An alpha-AA donates its amino group to alpha-ketoglutarte to produce glutamate and alpha-keto acid . This rxn is catalyzed by transaminase or aminotransferase .

Slide8:

-pyruvate is the alpha-keto acid of Alanine, while oxaloacetate is the alpha-keto acid of Aspartate.

-these reactions happen both ways according to the cellular needs.

Slide9:

Pyruvate can be used for gluconeogenesis or oxidized to A-CoA for TCA cycle .
ALT funnels to form Glutamate (preferred), so more Glutamate is produced

Slide 10:
-Glu is not a collector here.
note that Aspartate is not produced in the urea-cycle (not intermediate)

Slide 11 :
the amino group is not removed directly, but there is a mediator to facilitate the rxn .
-Pyridoxal phosphate (PLP) is the active form of V B6 .

- the pyridoxamine phosphate either reacts with oxaloacetate to form aspartate or with alpha-ketoglutarate to form glutamate.

Slide12:

Liver diseases as hepatitis , liver cirrhosis or any destruction of hepatocytes cause elevation of AST and ALT in the plasma.
ALT : more specific than AST (means it's special for liver and mostly found there)

AST: more sensitive (means that a small change in conc. can be detected easily).
eg/ ALT's conc. is elevated : most probably there's a liver disease whereas AST indicated that it might be a problem in the liver or somewhere else.

Bilirubin is a metabolite of hemoglobin need to be further metabolized in the liver . In liver diseases it's concentration is elevated and Jaundice occurs .

-Nonhepatic disease : especially AST.

Slide 13 :
-Glutamate dehydrogenase removes H atoms so it is oxidizing the substrates . That's why called oxidative deamination. It catalyzes both forward and reverse rxns .
-what determines which rxn happens rather than the conc. and the need of the cells is the coenzyme.

-NAD+ is the oxidized form of the coenzyme catalyzes the forward rxn
-NADPH is the reduced form catalyzes the reveres rxn.

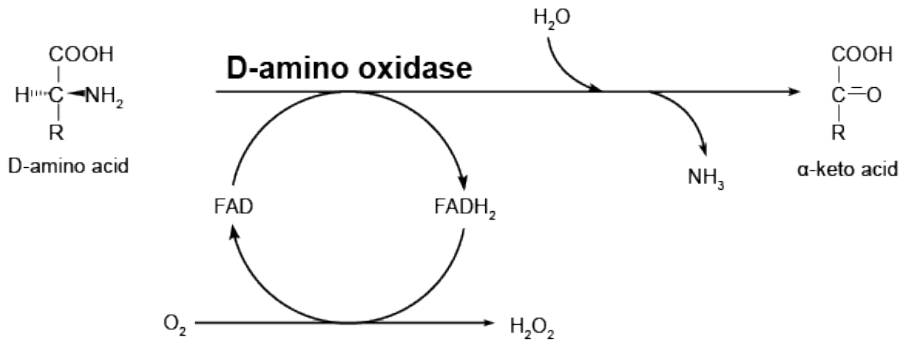
Slide 14 :

How this process is regulated? By the metabolism of AAs to produce other molecules or energy. For example when there's a high energy state the rxn doesn't proceed.

GTP indicates a high energy state . It is an allosteric inhibitor binds to a location other than the active site induces conformational change ,so it doesn't allow the binding and rxn to proceed.

ADP indicates a low energy state.

Slide 15 :
L-AAs are in our proteins.
we need to deal with D-AAs as we get them in antibiotics.



DAO : produces Alpha-keto acid , NH3(ammonia) and hydrogen peroxide.

Slide 16 : none

Slide 17 :

As discussed previously oxidative deamination is a source of ammonia.

Glutamine vs glutamate: gln has an amide group (carbonyl carbon with amino group) while glu has only carboxylic acid .

Glutamine is converted to glu by glutaminase(in the liver), whereas the reverse rxn catalyzed by glutamine synthetase (in most tissues).

Slide 18:

-Urea cycle happens only in hepatocytes, so I need to transport NH3 to the liver from other cells through blood carried on gln , then converting it to glu and NH3.

-NH3 released from the two mechanisms used in urea cycle.

Slide 19 :

-Urea cycle has many steps distributed in the mitochondria and the cytosol.

-at the mitochondria :

a) We insert NH3 from deamination with CO2 from Krebs cycle to synthesize the first molecule in the cycle (Carbamoyl phosphate) , this combination needs 2 ATP molecules.

b) Carbamoyl phosphate interacts with ornithine which is the final product of the cycle to produce citrulline . NOTE: this rxn is catalyzed by **OTC** (ornithine transcarbamaylase) .

c) citrulline is transported out of the mitochondria .

-at the cytosol :

d)citrulline enters the cycle with aspartate (That's why AST produces more Asp) to give argininosuccinate. This step need one ATP molecule .

e)argininosuccinate is split into arginine and fumarate . Fumarate is hydrated to malate which is oxidized to oxaloacetate and then transaminated to aspartate.

f) arginine is hydrolyzed to give the **cycle product UREA** and ornithine ready to repeat the first step.

Slide 20 : same as 19

Slide 21 :
we notice that the **urea cycle consumes energy.**

Slide 22 :
slide is enough

Good luck :D
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