Overview and Integration of Cellular Metabolism

Prof. Aritri Bir

Dr. B.C. Roy Multi-Speciality Medical Research Centre

Indian Institute of Technology Kharagpur

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Lecture 31: Digestion and absorption of Protein

Hello everyone. Welcome back to our lecture series session of Overview and Integration of Cellular Metabolism. So, we have completed the lipid metabolism as well as the carbohydrate metabolism. What we are going to start today is protein metabolism and today's class is of the topic the topic is Digestion and Absorption of Protein. Now in this class what we are going to discuss are the different levels of digestion of protein in GI tract, then what are the enzymes required for this digestion of protein. So, those are the proteases which are actually breaking down the ingested or dietary protein and finally, how those broken down peptide fragments or amino acids are absorbed from GI tract.

So, before starting the protein digestion absorption what you need to know is when we are talking about protein metabolism we are actually concentrating on the metabolism of amino acid. So, basically amino proteins are the chains of amino acids and those amino acids are joined by peptide bonds. So, when we are talking about catabolism of protein or digestion of protein. So, we are talking about how those joining peptide bonds are broken.

So, what is the enzyme which is causing breaking down of breakdown of peptide bonds that is peptidases or proteases. So, here we are going to discuss different types of proteases present in GI tract which is helping in digestion. Then protein undergo these proteins undergo constant turnover means the synthesis of protein and breakdown of protein they are balanced. So, this turnover of proteins are constant in our body. And finally, remember proteins are not the usual biomolecules which are generating energy, but it is important.

Important in terms of biosynthesis of important biomolecules as well as in conditions where other energy producing substrates like the main one carbohydrate glucose is depleted then the lipid store is depleted then comes the proteins from different tissue proteins muscle proteins or other proteins they are broken down to provide energy. So,

proteins are the last one in the group which provides which are required to provide energy in serious conditions. So, digestion of proteins are basically in our diet we are talking about the dietary proteins. Now, dietary proteins are of plant origin as well as animal origin and it is around 50 to 100 grams per day. Now, remember essential amino acids are actually obtained through diet remember why those are essential because those are not synthesized in our body.

So, those should be those essential amino acids should be consumed through diet whereas, non essential amino acids that are consumed through diet and those are also synthesized in our body. Now, endogenous proteins are also contributing to dietary are contributing to digestion and absorption of protein because those endogenous proteins are derived from digestive tract from where like digestive enzymes when they undergo turnover they generates few peptides or fragments of protein again the cells the digestive tract lining cells when they are degenerated they also seen they also donate to some pool of proteins in the digestive tract. So, those are also absorbed and that is around 30 to 100 grams per day. So, they are also digested and absorbed in our GI tract around 400 grams per day proteins are turned over in a adult healthy male. Then remember this digestion and absorption of protein this physiological phenomena is very very efficient most of the ingested proteins they are absorbed digested and then absorbed.

So, the loss through proteins are very low around 8 to 10 grams. Then we will discuss about the amino acid pool in our body. So, there is a pool of amino acid in our body which is in dynamic steady state that means, there is constant turnover of protein which is generating the amino acid pool and constant synthesis of protein and for that synthesis amino acid is actually taken from amino acid pool. So, that degradation and synthesis are occurring are actually contributing to the amino acid pool and that is dynamic and in steady state. Now why we are calling steady state because definitely the rate of synthesis and rate of degradation are constant.

So, the amino acid pool amount of that amino acid pool remains constant in our body. So, for digestion and absorption for digestion of protein it basically starts from the very beginning of cooking. Heating causes denaturation heating causes denaturation of proteins. So, basically that is also breaking down protein. Then it comes into our mouth now remember here in protein digestion mouth contributes very little or nothing because there is no proteolytic enzyme in our saliva only the chewing part that mechanical effort breaks a very little bit of protein in our mouth.

Then comes stomach there are enzymes like pepsin and renin remember renin this is not renin this is renin. Then pancreas in pancreas there are enzymes like trypsin, chymotrypsin, elastase and carboxypeptidase A and B. Then intestine in intestinal

enzymes the peptidases are amino peptidase di and tri peptidases. So, these are the important proteolytic enzymes present in our GI tract. Now, remember all the proteolytic enzymes they are actually present in our body in an inactive form which is known as zymosins.

Now why this is important why this is required this zymosins I mean the importance of why this proteolytic enzymes remains in inactive form. Because if just imagine if all the proteolytic enzymes are in active form they will digest all the adjacent cells cellular proteins all will be digested and broken down. So, basically this is for our safety that has been given by nature that all this proteolytic enzymes remains in zymosin form inactive form and when required only then they are activated by proteolytic cleavage or some modifications. Now proteolytic enzymes or peptidases are basically of two types one is endopeptidase another is exopeptidase. Endopeptidase it by its name it is evident that it is basically breaking down the peptide bonds present inside a protein molecule.

So, endopeptidase will breaks these bonds inside the protein molecule whereas, exopeptidase they will only break the terminal peptide bonds these are the suppose this is our N terminal end and this is our C terminal end. So, exopeptidase will break this terminal bonds only. Now those exopeptidase which are breaking amino terminal bonds they are known as aminopeptidase and those exopeptidase which are breaking carboxy terminal bonds they are carboxy peptidase and what are the examples of endopeptidase pepsin, trypsin, chymotrypsin, elastase all these are endopeptidase. Remember once again all these enzymes remain in inactive zymosin form. So, these are how the proteases work.

So, here endopeptidases are there which are breaking the inside peptide bonds whereas, the exopeptidase they are basically breaking the terminal bonds. So, we are moving on to digestion in stomach remember in stomach we have discussed there are 2 enzymes pepsin and renin. Now one very important feature of stomach content is it has a very low pH and that low pH is because of secretion of a mineral acid hydrochloric acid. Now what is the importance because the stomach environment is acidic around pH 2 to 3 that is the optimum pH required for the action of pepsin. So, this acidic pH is actually causing activation of pepsin.

So, pepsin remains in the inactive form that inactive form is known as pepsinogen. So, this acidic pH basically and when this HCL is actually released when there is chewing or gastric movement is it causes or food inside our stomach that causes the release of hydrochloric acid it signals for activation of the enzyme pepsin. So, pepsinogen is converted to pepsin and also the acidic environment causes acid causes denaturation of protein. So, apart from the enzymes hydrochloric acid present in stomach juice is

actually helping digestion of protein. Then comes the 2 important endopeptidase one is pepsin another is renin.

Now remember pepsin is secreted from the cheese cells of stomach. How pepsinogen is converted to pepsin by proteolytic cleavage. So, a segment of pepsinogen is removed from the N terminal end around 44 amino acid long fragment is removed and thus pepsinogen is converted to pepsin. Pepsin is the active form then pepsin catalyzes the hydrolysis of peptide bonds in the carboxy mostly in the carboxy terminal end of and between the and where the these amino acids are presents like phenylalanine, tyrosine, tryptophan, methionine. So, pepsin is breaking the carboxyl bonds of these amino acids and they are forming short fragments of protein or peptones.

Then comes renin, renin is also known as chymosine. Now renin is mostly secreted or active in infants they are not found they are not much active in adults or absent rather absent in adults. And renin is important for digestion because it is present in absent it is important for digestion of milk. So, it causes curdling of milk. So, milk protein casein is actually digested and converted to form parakezin.

Parakezin with calcium form parakezin net and after treatment by the renin the product is rather easy to be digested by pepsin. So, renin is actually helping in digestion of milk protein in case of infants. Then comes the digestion in small intestine. In small intestine there are endopeptidases like trypsin, chymotrypsin, elastases and exopeptidases like carboxypeptidases A and B. Now all these endopeptidases trypsin, chymotrypsin, elastases these are serine proteases.

Why? Serine amino acid is present in the active site of these all these endopeptidases and serine is actually taking part in substrate binding and catalysis in those endopeptidases. Now, the release of these enzymes or rather pancreatic juice is stimulated by peptide hormones cholocystokinin and pancreozyme. Now as we have already told that all the proteolytic enzymes are actually released and zymosanes. So, trypsin is actually where trypsin is present in the inactive form trypsinogen. Chymotrypsin is present in the inactive form chymotrypsinogen or elastase is present in the inactive from pro elastase.

Now pancreatic juice is alkaline around pH 8 and this alkaline pH or alkaline bile they are providing the optimum pH for actions or activations of these enzymes. So, now we are coming to trypsin. So, trypsin is basically activated by one intestinal microvilli membrane associated enzyme which is known as enterokinase. Now enterokinase once again causes the proteolytic cleavage in trypsinogen. So, there is removal of a hexapeptide segment from the N-terminal end of trypsinogen which causes the active

form formation that is trypsin.

Now trypsin it can go autocatalyzes. So, when trypsin is formed trypsin can induce its own activation as well as activation of different other enzymes like chymotrypsin is one very important enzyme which is activated by trypsin. Now trypsin is specific for the amino acid arginine and lysine. So, in the peptide chain when wherever there is arginine and lysine they are identified by trypsin and there is peptide bond breakage. Now remember why I told the importance of staying these peptideases in zymogen form because if those are activated they will cause digestion of the cells.

So, these type of these defect happens in case of acute pancreatitis. So, in pancreas the inactive trypsin or trypsinogen is stored. Now what happens in case of acute pancreatitis there is premature activation of trypsinogen. So, there is formation of trypsin now trypsin digest all the available proteins around it surrounding the released trypsin. So, it causes the auto digestion of pancreatic cells.

So, this is the problem if the enzymes remains in activated form in our body. So, that is the requirement of having zymogens. Then chymotrypsin remember chymotrypsin is activated by trypsin. So, basically the inactive form is chymotrypsinogen. Now chymotrypsinogen is activated by trypsin.

Now the trypsin actually breaks down here you can see before that I am just giving a brief feature telling the features of chymotrypsinogen molecule. So, chymotrypsinogen molecule is having 245 amino acid in it is chain then there are 5 disulphite bonds are there you can see these yellows are the disulphite bonds. Now when treated in presence of trypsin, trypsin causes a cleavage in amino acid 15 and 16 and here are is the 16. So, 15 is the arginine 16 is the isoleucine. So, there is a peptide bond breakage by trypsin in the chymotrypsinogen molecule.

So, what is formed is active chymotrypsin which is also known as p or pi chymotrypsin. But these two fragments here even after breakage these two fragments are attached by this disulphite bond. Then this pi chymotrypsin activates itself by forming two other fragments. Just see that if this pi chymotrypsin causes self digestion and releases two dipeptides.

So, here is one dipeptides. So, the amino acid 14 and amino acid 15 in a form of dipeptide they are released. So, these are serine and arginine and also amino acid 147th amino acid and 148th amino acid they are also released in the form of dipeptide those are threonine and asparagine. So, there is release of two dipeptides from the pi chymotrypsin molecules. So, what is formed is alpha chymotrypsin this is also another active form, but

remember the fragments are attached by the disulphide bonds. So, this is our active chymotrypsin from chymotrypsinogen where you can see only the first cleavage is run by trypsin whereas, the activated pi chymotrypsin then self activates by self digestion.

Now, chymotrypsin is specific for bond peptide bond breakage where aromatic amino acids are present. Then is elastase remember the elastase the progymogen form of elastase is pro elastase it is also activated by trypsin and it is specific for the amino acid glycine, alanine or serine. So, these are the endopeptidase then comes the carboxypeptidase carboxypeptidase remember it is exopeptidase it actually breaks the terminal carboxy terminal peptide bonds it remains in the xymogen form which is known as procarboxypeptidase. Zinc is required it is the cofactor for carboxypeptidase. So, basically this is one metallo enzyme then there are two types of carboxypeptidase and basically these carboxypeptidase A and B and why they are different because their targets are different.

So, carboxypeptidase A is specific for either aromatic or branch and amino acids whereas, carboxypeptidase B they are mostly targeted for the positively charged amino acid. So, these are our pancreatic enzymes for protein digestions. So, you can see these are the targets of the specific enzymes like pepsin you is targeted for amino acid tyrosine phenylalanine tryptophan or acetic amino acid glutamine glutamic acid then trypsin is targeted for basic amino acids arginine and lysine chymotrypsin are for aromatic amino acid elastase is for neutral amino acids like glycine serenalanine carboxypeptidase A they are target carboxypeptidase A is targeted for aromatic amino acid like tyrosine phenylalanine tryptophan or branch and amino acids then carboxypeptidase B for basic arginine and lysine amino acids. Then there is intestinal small intestinal enzymes now whatever digested whatever proteins are digested from stomach and pancreas they are finally, completely digested to give rise to free amino acid in small intestine by the enzymes aminopeptidase. So, this is one exopeptidase breaking the terminal amino terminal bond peptide bond and also dipeptidase and tripeptidase where the suppose this is the peptide molecule.

So, on action of dipeptidase this will be broken on action of tripeptidase this will be broken. So, they finally, forms the free amino acids. So, these are all about the enzymes for digestion of rather breaking down of dietary proteins. So, what we are getting are the free amino acids or short fragments of proteins. Now remember absorption is occurring absorptions of amino acids are there mostly if the dipeptides are tripeptides are by mistakes they are absorbed they sometimes give rise to allergic reactions.

Now the absorption of amino acids mainly occur in small intestine by from amino acid transporters. So, these are active transporters sodium dependent amino acid co transport

active transport means then is energy. So, those are ATP dependent transport system where breaking down of or hydrolysis of ATP provides energy. Now there are 5 different types of transporter based on the characters of amino acids. So, there is neutral amino acid transporter carrying alanine, valine, leucine, methionine, phenyl, phenylalanine, tyrosine, isoleucine.

Then there is basic amino acid transporter like lysine, arginine and cysteine. Amino acid transporter which carries proline and it carries glycine as well. Then acidic amino acid transporter like aspartic acid and glutamic acid and finally, beta amino acid that is beta alanine is carried by one specific amino acid transporter. So, there are 5 different types of amino acid transporter present in our GI tracts mainly in small intestine. Now one very important cycle is there with respect to absorption of amino acids and this cycle is known as Meister cycle or gamma glutamyl cycle.

Now absorption of amino acid in lumens, lumens like GI tract in intestine or sometimes in lumens of kidney or in the brain. So, there in those regions absorption of neutral amino acids are following the are dependent on Meister cycle. Now Meister cycle there is one very important tripeptide glutathione. Remember once again glutathione is a tripeptide formed by 3 amino acid glutamate, cysteine and glycine. So, this glutathione is known as gamma glutamyl cysteine glycine.

Remember once again this is one very important question gamma glutamyl cysteine glycine is glutathione. So, for glutathione synthesis what are the amino acids required? Glutamic acid, cysteine and glycine. Now glutamic acid or glutathione helps in absorption of neutral amino acid and neutral amino acid it forms a complex with glutathione that is glutamyl amino acid and glutamyl amino acid is finally, once again regenerating glutamate releasing you can see. So, what are basically what happens from the outside of the lumens from the our membranes through the membranes of the lumens this amino acid is transported inside by glutathione. Now they form the complex with the help of the enzyme GGT or GGTP that is gamma glutamyl peptidase to form glutamyl amino acid.

Now glutamyl amino acid once again regenerate amino acid once inside the cell with the help of the enzyme cyclotransference gamma glutamyl cyclotransference which finally, releases the amino acid and forms oxyproline. Oxyproline undergoes the cyclical formation of glutamate to glutamyl cysteine to finally, formation of glutathione. So, glutathione is once again regenerated and once again takes part in transport of amino acid. So, what happens via this cycle from outside the membrane amino acid is transported inside the cell and the imported enzymes are gamma glutamyl trans peptidase or transference and regeneration occurs via cyclotransference.

So, there is release of amino acid inside the cell. Now what are the clinical importance with this regard? So, here in if we go back that sometimes there is deficiency of this enzyme oxy 5 oxo proline is causing oxo proline accumulation. Now when this oxo prolines are accumulated they are secreted in urine which is known as oxo proline urea. Then another important thing as I told that food allergy there are different proteins which when absorbed in partially digested form they can give rise to allergenic reactions. Then there is transport defect if the transporters as I discussed in intestinal transporters are defective there is some diseases inherent diseases or inborn error of metabolism are related to those. So, one such important diseases is heart nerve disease where tryptophan absorption is defective which we will discuss in details in the metabolism of tryptophan.

Then immunoglycin urea it is related to the absorption defect or transport defect in amino acids like proline as well as glycine that will also be discussed in respective proline and glycine metabolism. And finally, cysteine urea when cysteine is absorbed there is absorption defect of cysteine where the dietary cysteines the amino cysteines are secreted in urine as well as those can be secreted in those can be deposited in the urinary tract causing stones or cysteinosis. Then protein absorption can be defective in case of partial gastrectomy. So, basically what happens in partial gastrectomy the stomach fails to release or the quantity of in storm enzymes proteolytic enzymes of stomachs are low. So, there is partial digestion of protein, pancreatitis, pancreatic enzymes are defective or carcinoma pancreas also cystic fibrosis where luminal secretion of enzymes are defective.

Then protein losing enteropathy so, basically this is a gastrointestinal tract absorption defect where excessive proteins are lost from GI tract causing protein losing enteropathy and there is hypoproteinemia in our body the protein content is low in our body. Then if we are talking about amino acid pool so, these are the till now we have discussed how proteins are supplied to the or amino acids are supplied to the amino acid pool. So, the this what we have discussed is about the dietary protein or supply, but how those proteins are cleared from cell by intracellular protein degradation. So, that is protein turnover. Now, protein turnover in our body is constant and around 1 to 2 percent daily turnover and this turnover rate is represented by t half or that is called half life.

So, half life or t half in case of protein turnover is the time taken by the protein where the protein concentration is just the half of its initial value. So, that is protein turnover rate. Now this protein turnover rate is variable or different for different types of enzyme. The like the proteins which are very quickly digested where the proteins functions should be terminated quickly like enzymes, hormones, transcription factors those are degraded very quickly their turnover rates are the half times are like in minutes. Whereas, few proteins like bone proteins their turnover rate is very high crystalline protein present in

lens throughout the life basically this crystalline protein turn is not turned over very slow rate of degradation of crystalline protein.

Now apart from that the normal physiological degradation of protein damaged or defective protein are degraded prematurely to clear those defective proteins from the cells. Now when these proteins are broken down they definitely gives rise to the constituents amino acids and those constituents amino acids are actually helping in formation of amino acid pool. Now, there are two types of intracellular protein degradation one is lysosomal proteolysis where the lysosomal enzymes hydrolysis are degrading protein and then ubiquitin proteosomal pathway. Now remember ubiquitin is a protein which tags the defective or damaged protein. Now that tagging of protein is a signal where proteosome proteosome identifies those proteosome is a complex structure a barrel like structure.

So, proteosomes identify identifies those tagged protein tagged by ubiquitin proteosome takes up those protein inside their barrel like structure and degrades those protein to the constituents amino acid. So, these are the two important degradation pathway of intracellular protein. So, this is our amino acid pool where amino acid pool is formed by either dietary protein which are absorbed in the form of amino acid then also the intracellular breakdown of protein body proteins like skeletal muscle broken down or different cells are broken down different enzymes hormones proteolyte protein peptide hormones when they are broken down or degraded they are finally, contributing to develop the amino acid pool. And this amino acid pool is actually utilized to form different proteins all the plasma proteins or body proteins apart from that non proteinaceous substances like nitrogenous substances ammonia then porphyrin creatinine those are also formed from this amino acid pool and also glycogen non protein non nitrogenous compounds like glycogen they are also fatty acid the fats they are also are helped to be synthesized from this amino acid pool.

So, here you can see how the amino acid pool contributes in our body. So, there is from the diet you can see formation of amino acid formation of amino acid pool then tissue protein when broken down they also contribute to the amino acid pool also the non essential fact amino acids which are formed inside our body they are also contributing to form our amino acid pool. Now, where this amino acid pool is utilized for formation of tissue proteins then also formation of non protein nitrogenous substances like purine pyrimidine creatinine porphyrin these are all formed from the amino acid then carbohydrate forms ATP's are also synthesized from this amino acids pool amino acid pool. So, this is the amino acid pool which remains in dynamic state constantly proteins are broken down or ingested amino acids or synthesized amino acids they are increasing the amino I mean contributing to form the amino acid pool, but once again those pools

are also are depleted or utilized for formation of different compounds. So, that state that phase of formation and utilization is balanced.

So, that is a steady, but dynamic state of amino acid pool. So, here the are the key points of this lecture that proteins while we are talking about proteins we are mainly concentrating in amino acid metabolism then digestion of proteins in our GI tract occurs mostly in stomach and intestine where mouth plays a very little role there are enzymes related to protein digestion like pepsin and renin present in stomach, trypsin, chymotrypsin, elastase, carboxypeptidases in pancreatic juice and aminopeptidases present in intestinal juice then we have discussed also amino acid pool. So, these are my references and see you in the next classes of protein metabolism.