* The 20S Proteasome
  + Quaternary structure of enzymes put together
  + 20S because sediment at certain rate?
  + Peptidase – recognises and cleaves peptide bond
  + Only degrade protein the the tag Ubiquitin
* Ubiquitin
  + Target proteins to be degraded by proteasome
  + Attach lysine of the protein through lipopeptide bond
  + Need ubiquitin ligase
  + Highly regulated in the cell
* Non-lysosomal protein
  + Compartmentalisation is an important factor
  + Major way cell signals is through compartmentalisation
  + Break down those not in the lysosome
  + Cells signal through compartmentalisation
  + The ones that are not in the lysosome need to be tagged
  + As long as they are in the lysosome, they are isolated
  + A condemned protein when ubiquitin attached – then become degraded
  + Require 4 tandem UQs – 1 not enough to condemn and degrade proteins
  + Not a random process
  + Targeted proteins get recycled in the lysosome
* Amino acid deamination
  + Aa generally – nitrogen gets secreted to urea – urea cycle
  + Carbon skeleton is recycled – glucose, ketone bodies, CO2,…
  + Free aa comes from… - in the gut – some other sources from degradation of protein
  + Breakdown aa get alpha-keto acid and ammonia – these 2 separate
  + Alpha-keto acid goes into the Krebs cycle
  + Ammonia, amide, nitrogen group – excreted, removed, transferred
  + Transamination interconverts
  + Glutamate transfers ammonia to kidney
* PLP – vitamin B6
  + Important cofactor
  + Charges – phosphate group – and CHO – gives it the ability to assist enzyme to break bonds and transfer nitrogen
* Transamination
  + Transfer NH3+ to alpha-keto acid to make alpha-amino acid
  + Equilibrium reaction
  + Need PLP
  + Not regulated cuz Keq = 1
* Degradation of aa
  + Alanine to glutamate
  + Aminotransferase
  + Get rid of excess aa – need to go to glutamate – glutamate dehydrogenase makes NH4+
  + In animals, glutamate dehydrogenase is UQ – in all cells with mitochondria eg. except red blood cell
  + Glutamate degraded by glutamate dehydrogenase – make ammonia
  + Allosterically controlled – inhibited by GTP – low energy in cell, take out carbon from protein and extract carbon from it – high energy inhibit that process so cannot produce carbon component of aa
* Glutamate is oxidatively deaminated
  + Cofactors need to be there
  + GDH
* SGOT and SGPT
  + Test on speculation of what happened if sth is mutated – probably won’t be tested
* Transaminases use PLP
* In most tissues, glutamate is transferred to glutamine, glutamine transported to liver and converted to urea to get rid of NH4
  + Excess level of glucose or aa, it gets broken down to make alanine and go into liver to make urea
* Carbamoyl phosphate synthetase
  + Ammonia is toxic in high levels
  + Animals assimilate ammonia by reacting with carbamoyl phosphate
  + Carbamoyl phosphate has charges so can carry electrons
* Urea cycle
  + Very similar to Krebs cycle
  + A little simpler than Krebs cycle
* Krebs-Henseleit urea cycle
  + Exact same cycle like the urea cycle but what is happening in the mitochondria and what is happening in the cytosol – connect to the CAC
  + Urea is very stable and not reactive – act as a buffer to some extent
* Convert ammonia to less toxic form
  + Urea and uric acid – less toxic
  + Ammonia and NH3+ from asparate combine to make urea
  + Urea + fumarate = malate
  + Uric acid is more common in birds – excrete quite easily
  + Aquatic animals simply excrete ammonia because there is so much water
  + That is why we wash fish before eating – has ammonia on skin
  + Urea is highly soluble in water – NH2 can form hydrogen bonding with water
* Transamination is necessary to know
* Urea cycle is linked to gluconeogenesis and CAC
  + Transamination – alpha-Keto acid and alpha-amino acid
  + Fumurate to Malate to Oxaloacetate
  + Carbamoyl phosphate – first step in urea
* These aa generated from Krebs cycle
* Degradation to pyruvate
  + Last step is always transamination
  + One enzyme-based chemotherapy reaction is asparaginase – stop asparagine uptake by cancer cells