

# **AMINO ACID METABOLISM**

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**FMUI**

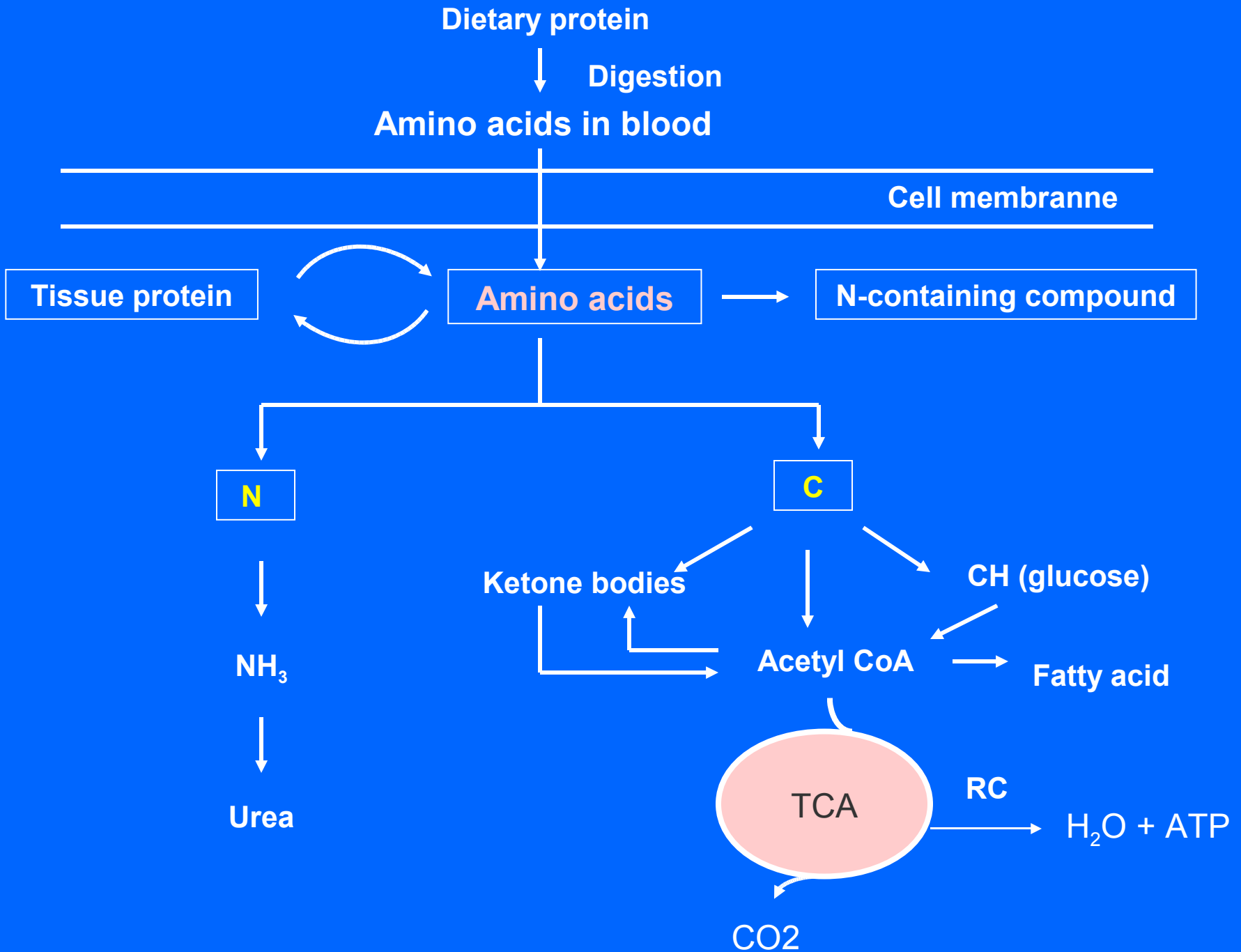
Amino acids – derived from dietary protein – absorbed from intestine through blood – taken up by tissues – used for

- ✎ biosynthesis of body protein
- ✎ oxidized to yield energy

Body protein always undergo turnover – constantly being synthesized and degraded

The AA released by body protein breakdown – enter the same pool of AA as the AA from the diet

AA also used for synthesis of N-containing compound



- ❧ Metabolism of amino acid - more complex compared to carbohydrate and lipid metabolism
- ❧ In normal diet, 60-100 g proteins- most are used for synthesis of proteins in liver and other tissues
- ❧ Excessive amino acids in the diet – converted to glucose (energy) → fatty acid → t a g (energy depot)

# Amino acid required for

- ✿ Biosynthesis of proteins
- ✿ precursor for N compounds
- ✿ oxidized - N atom → urea
  - C atom → - CH (glucose)
    - acetyl CoA – ketone bodies,  
fatty acid
    - non essential amino acid

Amino acids – 20 AA forming protein in nature

- ❖ Essential AA – must be present in the diet – can not be synthesized
- ❖ Non essential AA – can be formed by transamination of metabolic intermediates

# 11 from 20 AA-forming protein – can be synthesized in our body (non essential AA)

➤ 10 AA → can be synthesized from glucose

- ser - asn
- gly - glu
- cys - gln
- ala - pro
- asp - arg

➤ 1 AA → synthesized from essential AA

phe → tyr

➤ 9 AA → essential → must be present in our diet → its C atom - can not be synthesized

- lys - trp
- ile - phe
- leu - met
- thr - his
- val - \*arg

(L I L T V T O P M H A)

- Arg → semi essential  
children → essential  
adult → synthesis from urea cycle



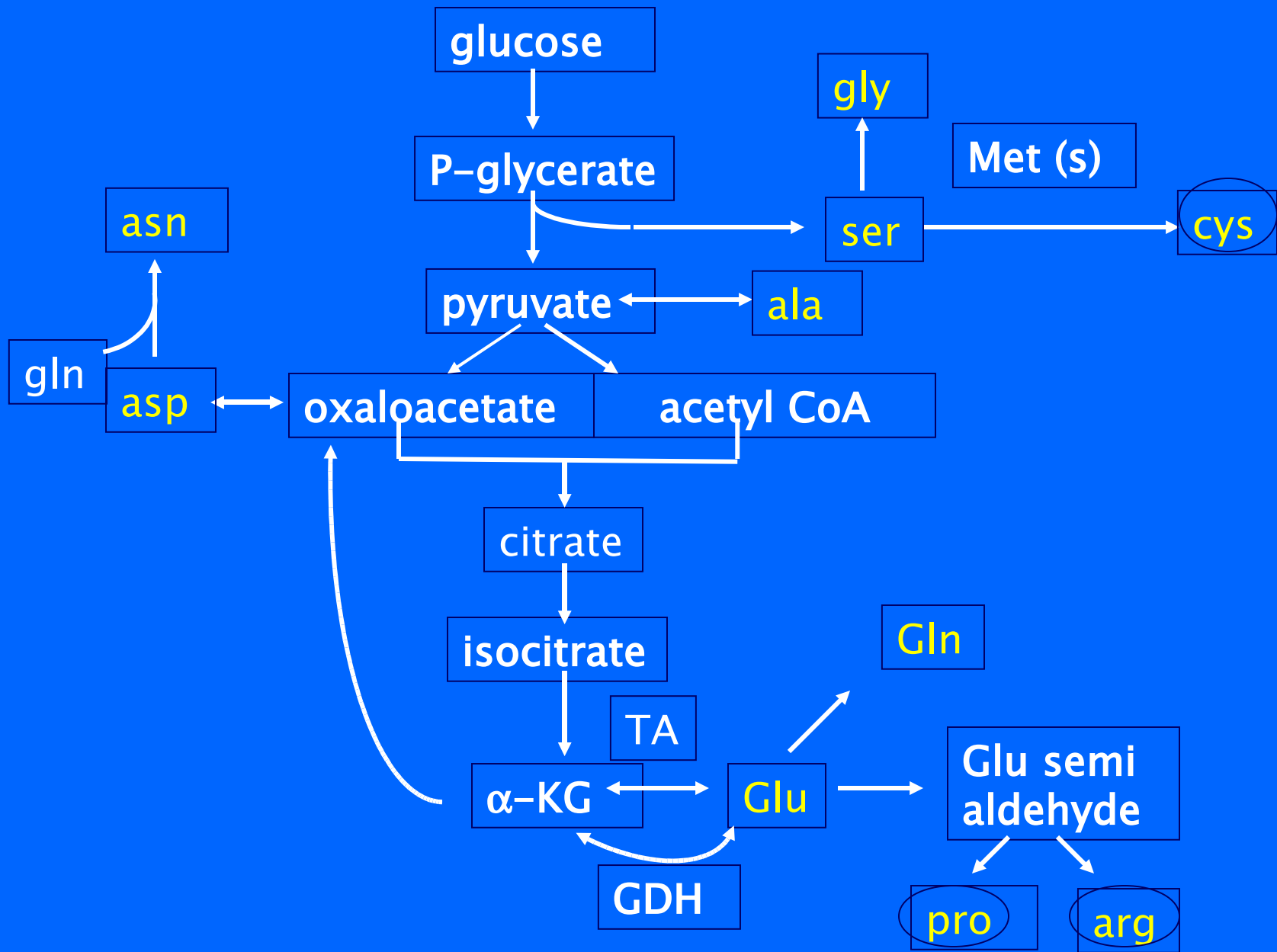
## DEGRADATION of AMINO ACIDS

- ☛ their carbons converted to
  - $\text{CO}_2$
  - compounds that produce glucose in the liver (pyruvate,  $\alpha$ -KG, succ CoA, fumarate, oxaloacetate)
  - ketone bodies
- ☛ glucogenic a a - if their C converted to glc
- ☛ ketogenic a a - if their C converted to acetyl CoA or acetoacetate

# METABOLISM OF CARBON ATOM AA

## 11 non essential AA

- ❖ 10 AA – can be formed from glucose – through intermediate of glycolysis and TCA
  - 4 AA – from **glycolysis intermediate**
    - ser
    - gly
    - cys
    - ala
  - 6 AA – from **TCA cycle intermediate**
    - glu, gln, pro, arg – from  $\alpha$ -KG
    - asp, asn – from oxaloacetate



In fasting

• most of AA  $\rightarrow$  pyruvate, intermediate of TCA cycle, acetyl CoA  $\rightarrow$  formed glucose or ketone bodies  $\rightarrow$  blood  $\rightarrow$  energy for the tissues  $\rightarrow$   $\text{CO}_2 + \text{H}_2\text{O} + \text{ATP}$

- ❖ AA synthesized from intermediate of glycolysis (non essential A) - produced` pyruvate on degradation
- ❖ A A synthesized from intermediate of Krebs cycle - produced this intermediate during degradation

# Glucogenic amino acids

- ✿ **tryptophane** → produced alanine → converted to pyruvate → glucose
- ✿ **methionine, threonine, valine, isoleucine** → succinyl CoA → glucose
- ✿ **Phenyl alanine** → converted to **tyrosine** → fumarate → glucose

## Glucogenic and ketogenic amino acids :

- tryptophane, isoleucine, threonine → acetyl CoA
- phenyl alanine → acetoacetate

## Ketogenic amino acids :

- lysine, leucine

- ☞ **During fasting** – muscle proteins were degraded to amino acids – some were oxidized to produce energy and converted to ala and ser
- ☞ In gut cells – glu converted to ala
- ☞ Ala & other amino acids – enter the liver
  - **nitrogen converted to urea**, excreted in the urine
  - **carbons converted to glucose and ketone bodies** – oxidized by various tissues for energy



- ✂ before the carbon skeleton of amino acids are oxidized, the nitrogen atom must be **removed**
- ✂ nitrogen atom from AA - formed **ammonia (NH<sub>3</sub>)**  
– **toxic to the body**
- ✂ in liver NH<sub>3</sub> and **–NH<sub>2</sub> group** from AA - converted  
to **urea**

## ROLE of GLUTAMATE in METABOLISM of AMINO ACID NITROGEN

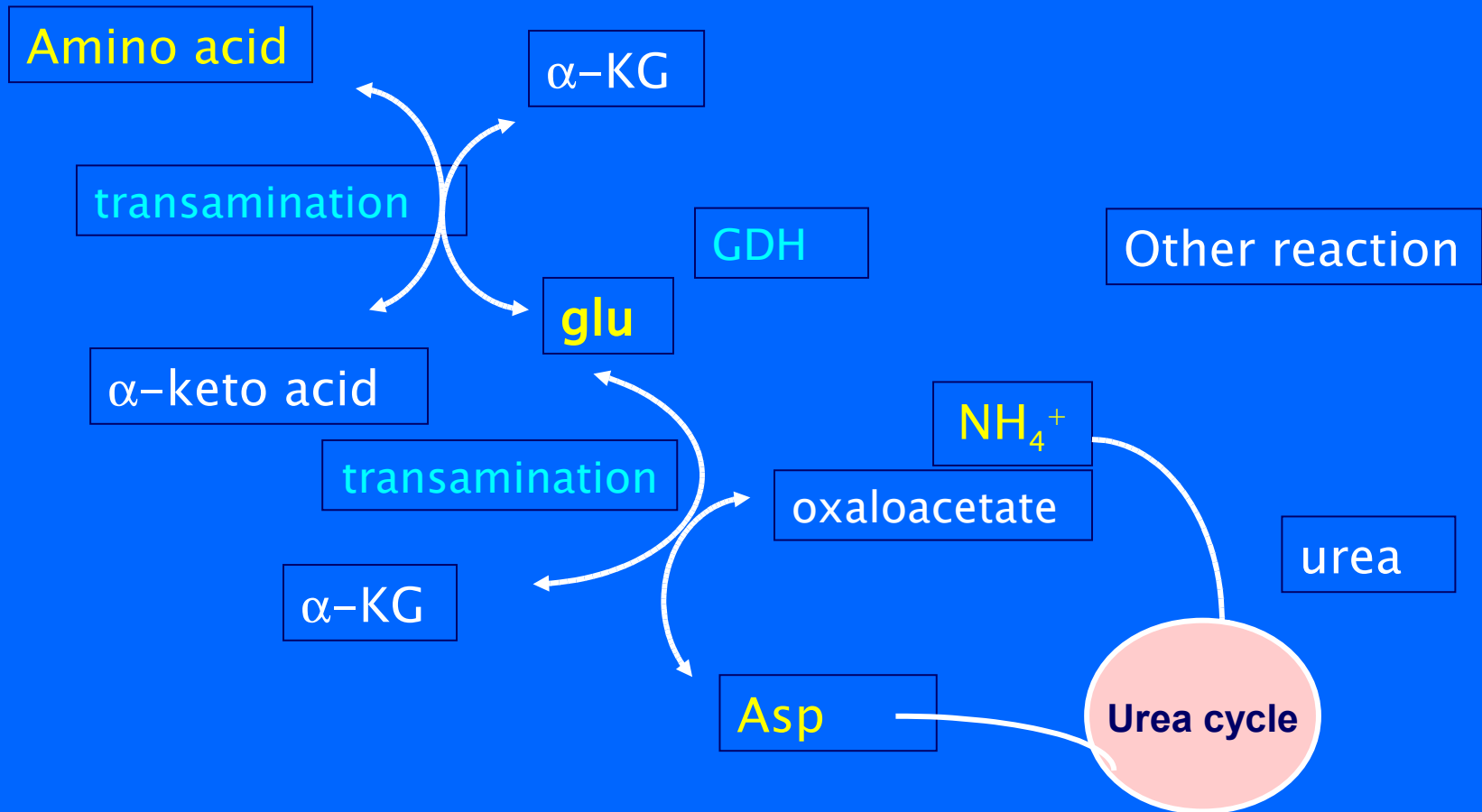
- ☛ glu play role in synthesis and degradation of amino acids

### Role of glutamate in AA synthesis

- ☛ glu obtains N from other amino acid by
  - transamination reaction
  - from  $\text{NH}_4^+$  by glu dehydrogenase reaction
- ☛ transfer  $\text{NH}_2$  group from glu to  $\alpha$ -ketoacid → produce corresponding amino acid

## Role glutamate on AA degradation

- ✂ glu collect N from other amino acids by transamination reaction
- ✂ some of this N - released as  $\text{NH}_3$  by glu dehydrogenase reaction



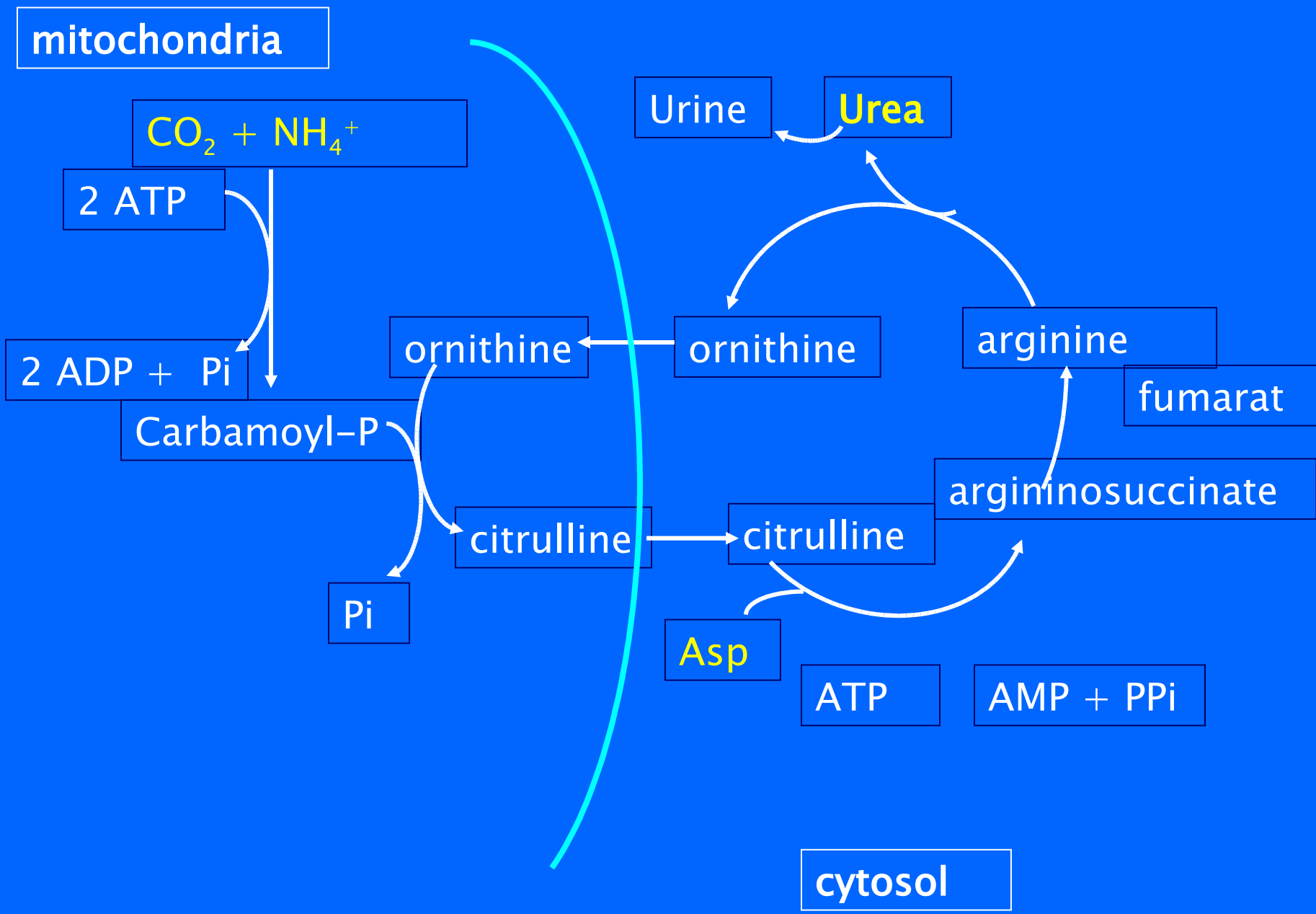
## Role of glutamate in metabolism of AA nitrogen

- ❧ Glutamate can collect nitrogen from other amino acids (from transamination reactions) – then release  $\text{NH}_3$  via glutamate DH reaction
- ❧ His - directly deaminated to form  $\text{NH}_4^+$
- ❧ Ser and thr - dehydrated, need PLP - form  $\text{NH}_4^+$
- ❧ Gln and asn - deamidated - form  $\text{NH}_4^+$ , glu and asp, catalyzed by glutaminase / asparaginase

# UREA CYCLE

## STEPS

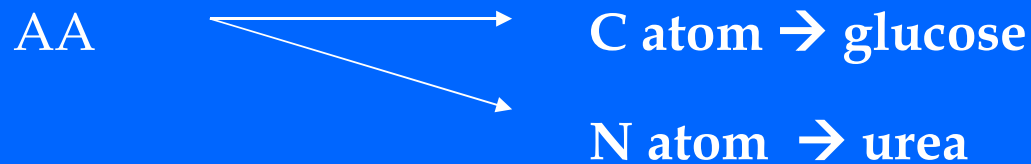
- ☞ **synthesis of carbamoyl phosphate** ( in mitochondria) from  $\text{NH}_4^+$ ,  $\text{CO}_2$  and ATP
- ☞ **production of arginine**
  - carbamoyl P + ornithine  $\rightarrow$  citrulline
  - citrulline transported across mitoch. membrane -enter cytosol
  - in cytosol, citrulline + aspartate  $\rightarrow$  arginino-succinate, cleave by argininosuccinase  $\rightarrow$  fumarate + arginine
- ☞ Arginine cleave by arginase  $\rightarrow$  **urea + ornithine**  
ornithine transported into mitoch, for another round of the cycle



# Urea excretion in fasting

- ☞ **Fasting** – important role of liver to maintain blood glucose

AA from muscle protein → substrate for gluconeogenesis



→ **urea excretion** ↑ in fasting state

- ☞ **Prolonged fasting**

Brain → did not depend on glucose, use ketone bodies as energy

→ sparing blood glucose – less muscle protein is cleaved to

provide AA for gluconeogenesis → **urea excretion** ↓

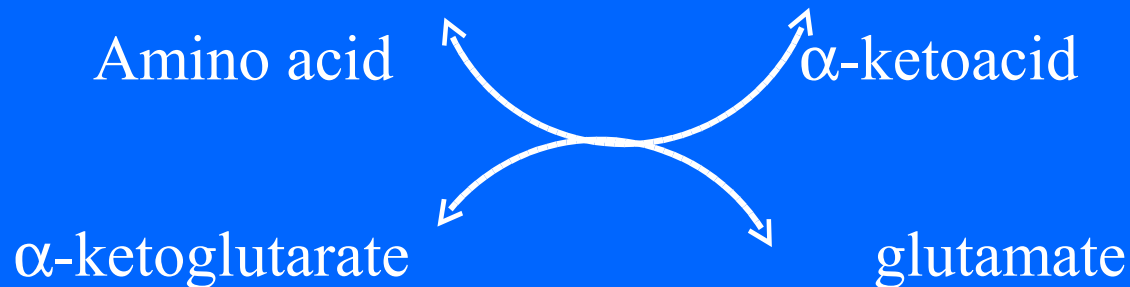


# Transfer of $-NH_2$ group between AA

- Non essential AA – can be synthesized from its keto acid (if needed), via transfer of  $-NH_2$  group from AA to keto acid, catalyzed by **transaminase** or aminotransferase
- Transfer of  $-NH_2$  also occur in degradation of AA
- Reaction is reversible – in hyperammonemia – disturbance in N excretion - supplementation of keto acid in the diet
- Example of transaminase – SGOT (=AST), SGPT (=ALT)

## Transamination reaction .

- the major process for removing nitrogen from amino acids
- nitrogen transferred from original amino acids to  $\alpha$ -ketoglutarate  $\rightarrow$  glutamate +  $\alpha$ -ketoacid, catalyzed by transaminase, pyridoxalphosphate (PLP) as cofactor



- all amino acids ( excepts lys & thr ) – can undergo transamination

## Oxidative deamination.

- nitrogen of certain amino acids released as ammonia ( $\text{NH}_3$ ) or ammonium ( $\text{NH}_4^+$ )
- Glutamate (glu) oxidatively deaminated by glutamate dehydrogenase (Glu DH), produces  $\text{NH}_4^+$  +  $\alpha$ -ketoglutarate
  - $\text{NAD}^+$  or  $\text{NADP}^+$  as cofactor
  - occur in mitochondria

☛ Enzymes important in the process of inter conversion of amino acids and removing nitrogen

- transaminase
- glutamate dehydrogenase
- deaminase

☛ Conversion of amino acid nitrogen to urea – occur mainly in the liver – through urea cycle – from precursor

- $\text{NH}_4^+$
- $\text{CO}_2$
- ATP
- nitrogen of aspartate

# NITROGEN BALANCE

- ☞ Healthy adult - **N balance N** (N intake = N excreted as urea))
- ☞ In well fed state - N excreted - come from
  - Intake of protein >> or
  - Normal “turnover” protein
- ☞ **Positive N balance** → **N intake > N excreted**
  - Growth & development
  - Pregnancy
  - Convalescence
- ☞ **Negative N balance** → **N excreted > N intake**
  - Starvation
  - Disease
  - Deficiency of essential AA

## N- containing product from AA

- ☛ Cellular protein
- ☛ Hormone (tyroxine, epinephrine, insulin)
- ☛ Neurotransmitter
- ☛ Creatine-P
- ☛ Heme of Hb, Mb, cytochrome
- ☛ Melanine pigment
- ☛ Purine and pirimidine base

# N-CONTAINING COMPOUND FROM AMINO ACIDS

## 1. Creatine

- synthesized from gly, arg and S-adenosylmethionine (SAM)
- + ATP  $\rightarrow$  creatine P ( stores and transport high energy phosphate within cells)
- creatine P spontaneously  $\rightarrow$  creatinine (excreted in urine)
- serum creatinine - indicator of GFR of the kidney
- urinary creatinine - assessing the quantity of other compounds excreted in the urine

## 2. Glycine

used for conjugation reaction with other compounds (in phase II xenobiotic metabolism) - increased water solubility - easier to excrete in the urine (bile salts, metabolites, drugs)

## 3. Heme

produced by condensation of gly and succ CoA →  $\delta$ -aminolevulinic acid, precursor of heme



#### 4. Purine base ring

entire gly molecule incorporated into ring + other N provided by gln and asp + CO<sub>2</sub> + tetrahydrofolate

#### 5. Pyrimidine base ring - formed from asp + carbamoyl P

#### 6. Neurotransmitter, hormone, pigment

γ-aminobutyric acid (GABA), histamine, serotonin, dopamine, norepinephrine, epinephrine, insulin, thyroid hormone, NO<sub>2</sub>, melanine

# INTEGRATION OF METABOLISM

## In well fed state

- ✿ **After meal** – fuels are oxidized – to meet our energy needs
- ✿ Any excess of fuel is stored
  - mainly as **triacylglycerol** in adipose tissue
  - as **glycogen** in muscle and liver
- ✿ **Amino acids** – converted to body proteins, particularly in muscle

## During fasting

- ☛  $\pm$  1 hour after meal – blood glucose  $\downarrow$  - insulin  $\downarrow$ , glucagon  $\uparrow$
- ☛ Liver glycogenolysis  $\uparrow$  - supplying glucose to the blood
- ☛ Adipose tissue lipolysis  $\uparrow$  - glycerol  $\uparrow$  and FFA  $\uparrow$  in blood
- ☛ FFA – major fuel that oxidized by muscle and liver
- ☛ Liver use FA to produce ketone bodies – to the blood – taken up by extrahepatic tissues for energy
- ☛ Brain & erythrocyte – use glucose as energy

## As **fasting progress**

- ❧ liver produce glucose from gluconeogenesis – from substrate glycerol, lactate, glucogenic amino acid
- ❧ If C atom of AA converted to glucose – the N atom converted to urea → urea excretion ↑

## **Prolonged fasting**

- ❧ Muscle decreases its use of ketone bodies – ketone bodies ↑ in blood
- ❧ Brain oxidizes ketone bodies as energy – brain need less glucose – liver decreases its rate of gluconeogenesis – muscle protein is spared – because degradation of protein to AA ↓ → urea excretion ↓

Thank you