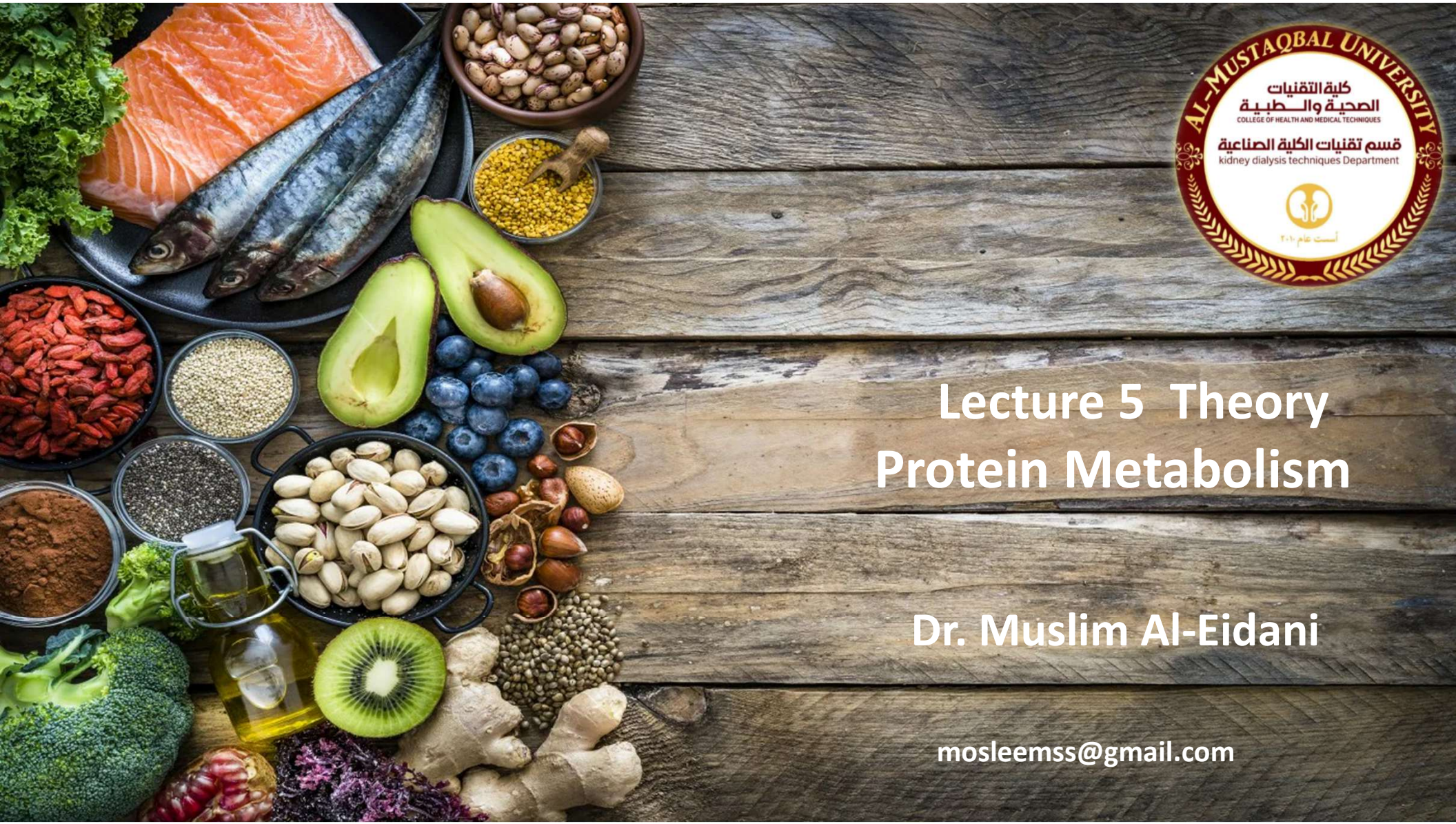

Lecture 5 Theory
Protein Metabolism

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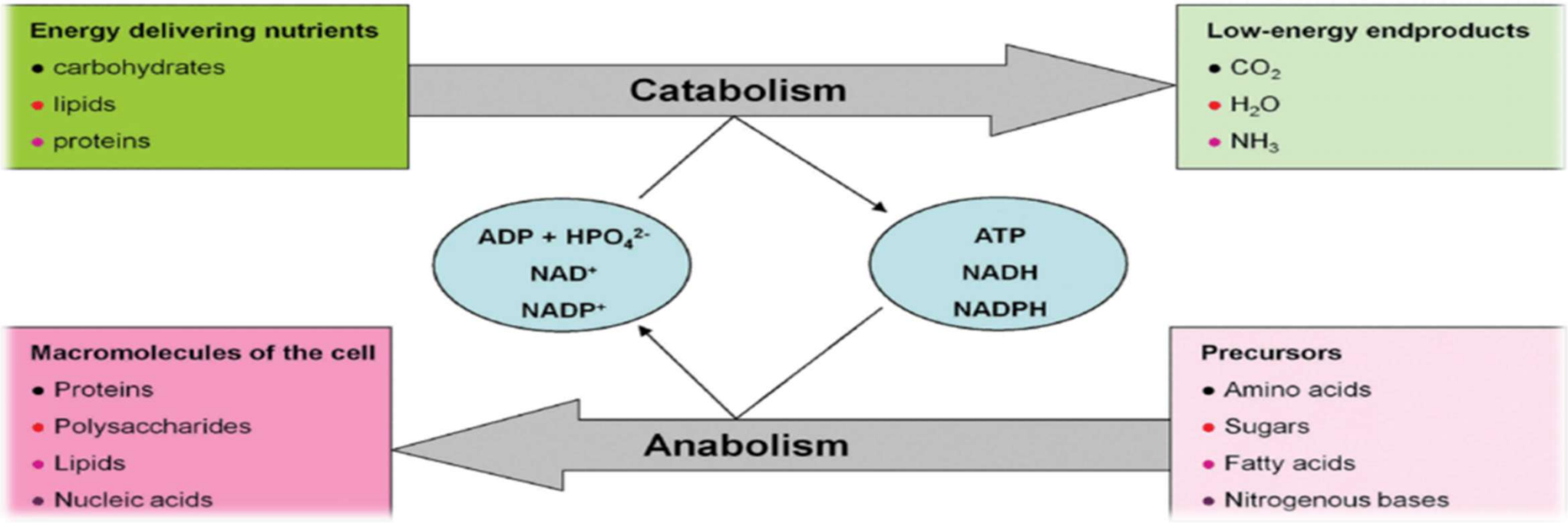
What is Protein Metabolism?

the biochemical processes responsible for the synthesis of proteins and amino acids (anabolism), and the breakdown of proteins by catabolism.



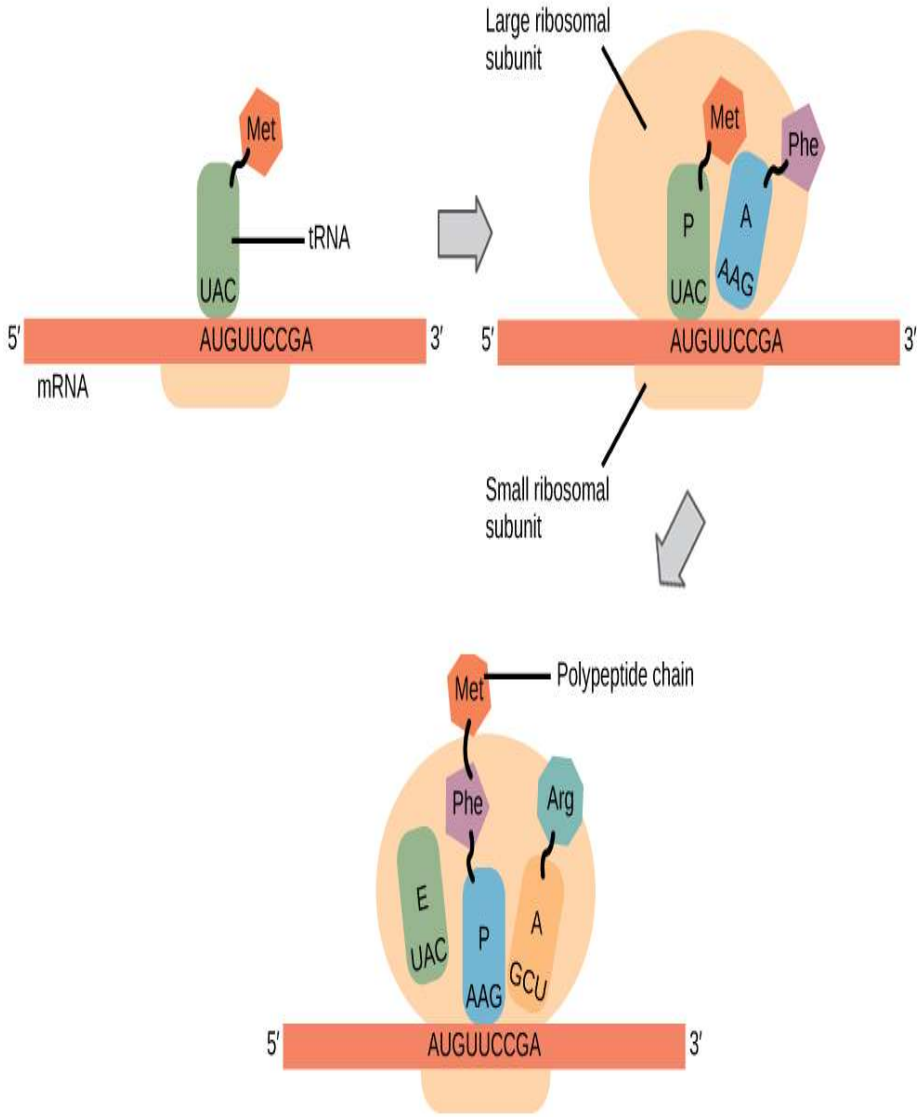
Protein Synthesis

Transcription

1. DNA unwinds in the **nucleus**
2. **RNA polymerase** binds to promoter region
3. mRNA strand synthesized (5' to 3')
4. mRNA undergoes processing and export to cytoplasm

Translation

1. Ribosome binds to mRNA in the **cytoplasm**
2. tRNA brings amino acids to ribosome
3. **Peptidyl transferase** forms peptide bonds
4. Polypeptide chain elongates until stop codon



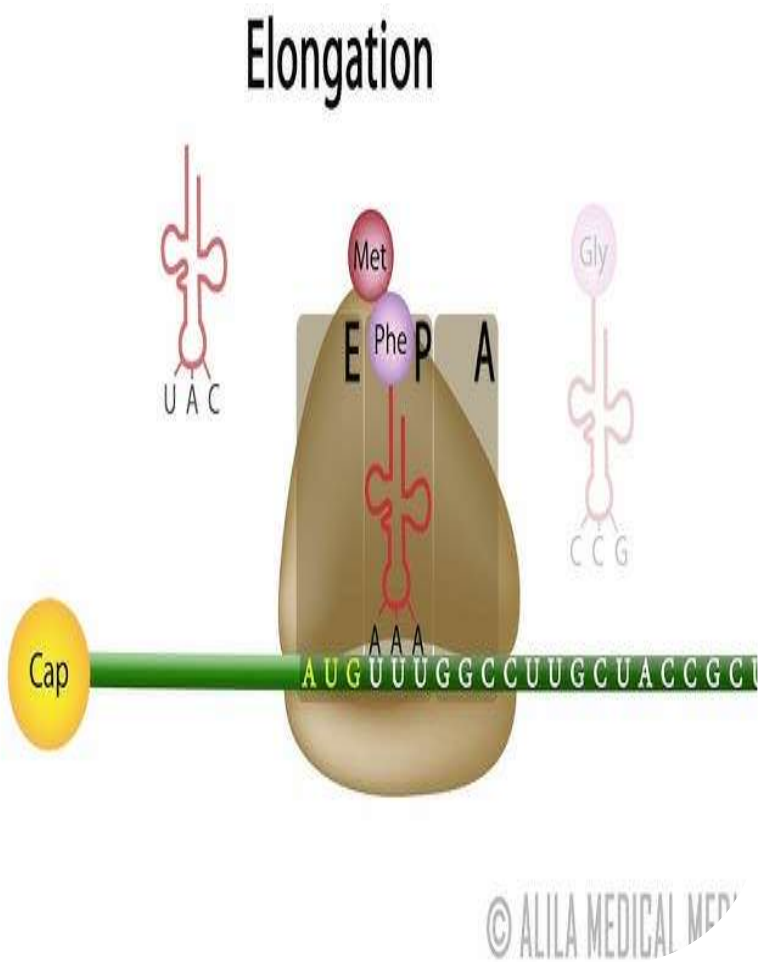
Enzymes in Protein Synthesis

Peptidyl Transferase

- **Type:** Ribozyme (RNA-based enzyme)
- **Location:** Large ribosomal subunit
- **Function:** Catalyzes peptide bond formation
- **Structure:** Entirely composed of rRNA
- **Process:** Links amino acids during translation

Other Key Enzymes

- RNA Polymerase
- Aminoacyl-tRNA Synthetase
- Release Factors
- Initiation Factors



Protein Catabolism

1 Stomach

- **Enzyme:** Pepsin
- Proteins → Polypeptides

2 Pancreas

- **Enzymes:** Trypsin, Chymotrypsin
- Polypeptides → Smaller Peptides

3 Small Intestine

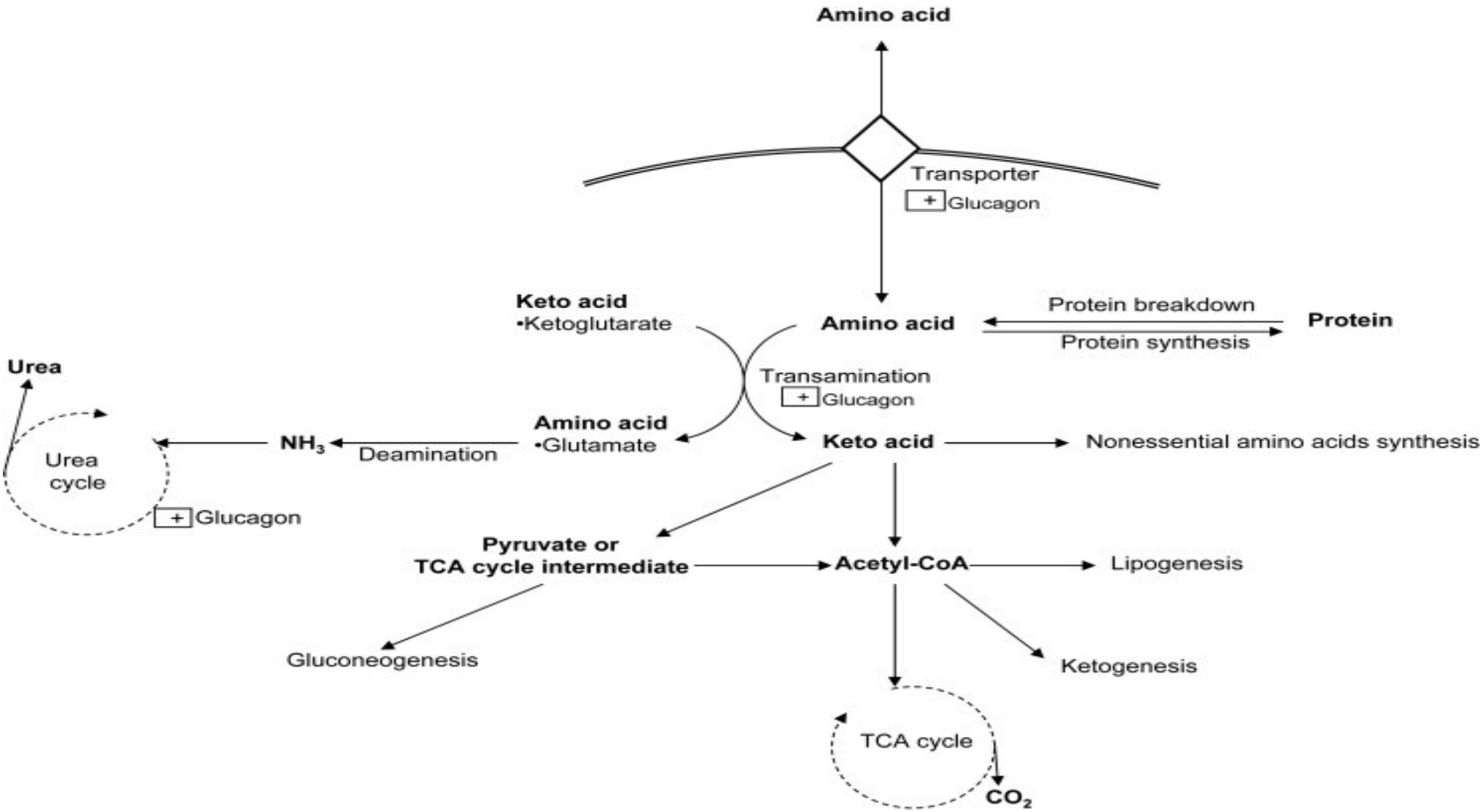
- **Enzymes:** Peptidases
- Peptides → Amino Acids

4 Cellular Level

- **Enzymes:** Transaminases
- Amino Acid Processing

Fate of Amino Acids

- **New Protein Synthesis**
- **Energy Production**
- **Gluconeogenesis**


Amino acid
Transporter
+ Glucagon
Keto acid
•Ketoglutarate
Amino acid
Protein breakdown
Protein synthesis
Protein
Transamination
+ Glucagon
Urea
Urea cycle
+ Glucagon
NH3
Deamination
Amino acid
•Glutamate
Keto acid
Nonessential amino acids synthesis
Pyruvate or
TCA cycle intermediate
Acetyl-CoA
Lipogenesis
Gluconeogenesis
Ketogenesis
TCA cycle
CO2

CKD and Uremic Toxins

Chronic Kidney Disease Impact

Decreased Function

Reduced excretory capacity → **toxin accumulation**

Uremic Toxins

Produced by **protein & amino acid breakdown**

Muscle Protein

Largest store of protein & amino acids

Imbalance

CKD patients have **disrupted balance** between protein breakdown & synthesis

Consequences of Uremic Toxins

- **Muscle breakdown** produces more uremic toxins
- Creates **vicious cycle** of muscle loss
- Normal adults break down **3-5%** of body proteins daily
- High dietary protein **overworks** damaged kidneys

Uremic Syndrome

Body Mass Loss **Weakness** **Fatigue**

Poor Wound Healing **Heart Disease** **Inflammation**

Protein Recommendations for Non-Dialysis CKD Patients

Reduced Uremic Toxins

Less dietary protein → **less breakdown** → **fewer toxins**

Gut Microbiome

Dysbiotic bacteria convert protein to **uremic toxins** in intestines

Electrolyte Balance

Protein-rich foods contain **sodium, potassium, phosphorus** → toxic in excess

Acid Reduction

Protein breakdown produces **acid** → causes metabolic acidosis in CKD

Additional Concerns with High Protein

- High protein intake → **excess salt** → high blood pressure
- **Phosphate accumulation** → blood vessel calcification
- Phosphates **antagonize** kidney-protective medications
- Metabolic acidosis → **bone weakening** and muscle breakdown

Protein-Energy Wasting Prevention

Protein restriction must be carefully managed to prevent muscle loss and malnutrition

Dietician

Nephrologist

Protein Recommendations for Dialysis-Requiring CKD Patients

Protein Loss During Dialysis

Hemodialysis: 10-12g amino acids per session

Peritoneal Dialysis: 5-15g albumin daily

Different Approach

Unlike non-dialysis CKD patients, dialysis patients need **higher protein intake**

To compensate for losses during dialysis procedures

Protein Intake Recommendation

For patients on dialysis, higher protein intake is recommended compared to non-dialysis CKD patients

> 1.2 g/kg body weight/day

This contrasts with protein restriction advised for non-dialysis CKD patients

Enzymes in Protein Catabolism

Pepsin

- **Location:** Stomach
- **Function:** Proteins → Polypeptides
- **Active pH:** 1.5-3.5

Trypsin

- **Location:** Small Intestine
- **Function:** Polypeptides → Peptides
- **Activation:** Trypsinogen → Trypsin

Chymotrypsin

- **Location:** Small Intestine
- **Function:** Peptides → Smaller Peptides
- **Activation:** Chymotrypsinogen → Chymotrypsin

Peptidases

- **Location:** Small Intestine
- **Function:** Peptides → Amino Acids
- **Types:** Aminopeptidases, Carboxypeptidases

Transaminases (Aminotransferases)

- **Function:** Transfer amino groups between amino acids and keto acids
  - **ALT (Alanine)**
  - **AST (Aspartate)**

The Urea Cycle

The urea cycle converts toxic **ammonia** into **urea** for excretion. Occurs primarily in the **liver** and to a lesser extent in the **kidneys**.

1. **Carbamoyl Phosphate Formation**
   $NH_3 + HCO_3^- + 2ATP \rightarrow$ Carbamoyl Phosphate
   - Mitochondria (CPS1 enzyme)

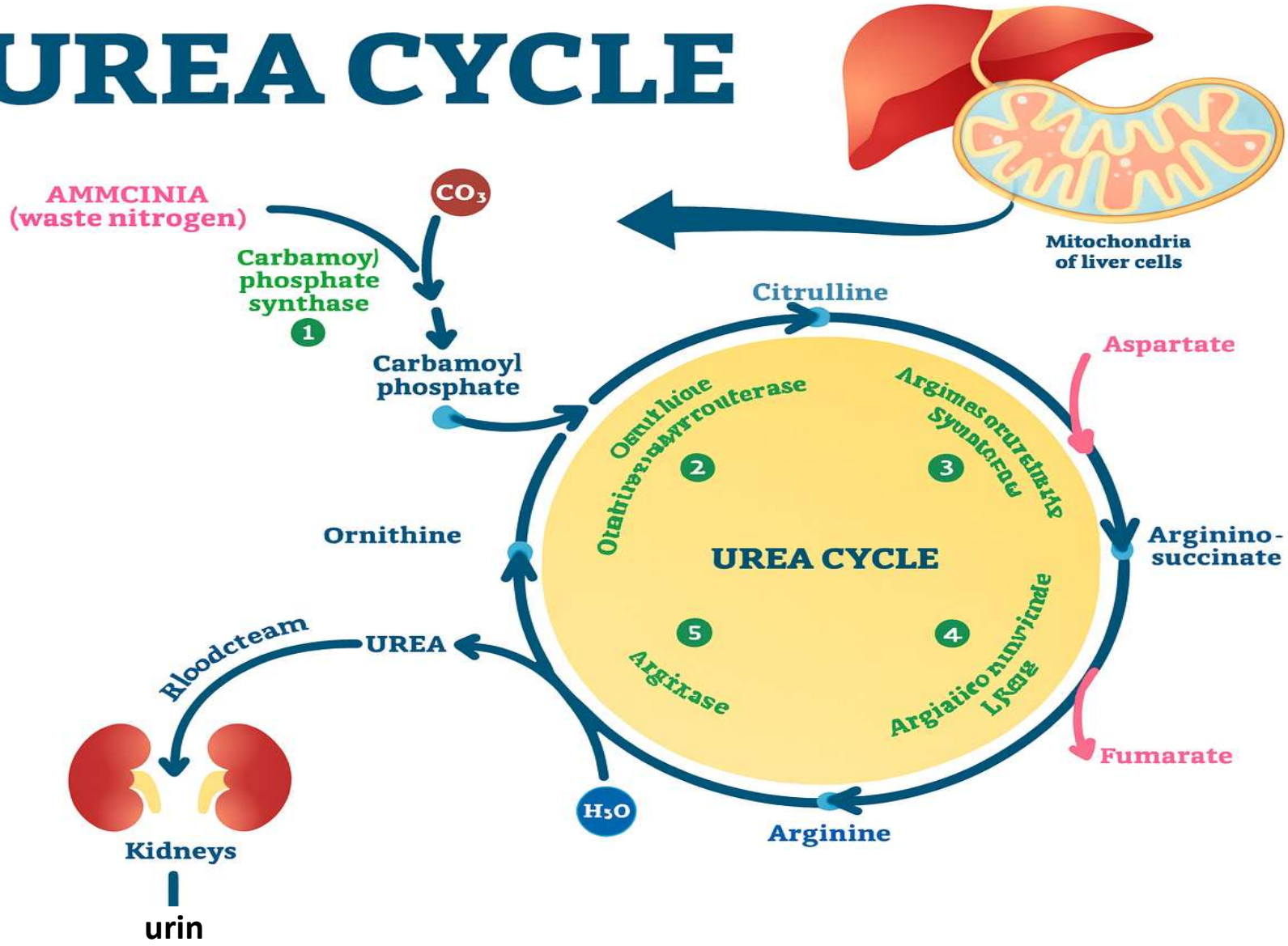
2. **Citrulline Formation**
   Carbamoyl Phosphate + Ornithine → Citrulline
   - Mitochondria (OTC enzyme)

3. **Argininosuccinate Formation**
   Citrulline + Aspartate + ATP → Argininosuccinate
   - Cytosol (ASS enzyme)

4. **Arginine Formation**
   Argininosuccinate → Arginine + Fumarate
   - Cytosol (ASL enzyme)

5. **Urea Formation**
   Arginine + H_2O → Ornithine + Urea
   - Cytosol (ARG1 enzyme)

UREA CYCLE


AMMCINIA
(waste nitrogen)
CO_3
Carbamoyl
phosphate
synthase
1
Carbamoyl
phosphate
Mitochondria
of liver cells
Citrulline
Aspartate
2
3
UREA CYCLE
Ornithine
Arginino-
succinate
5
4
UREA
Fumarate
H_3O
Arginine
Kidneys
urin

Hormonal Regulation of Protein Metabolism

Insulin

- \+ Stimulates **protein synthesis**
- − Inhibits **protein breakdown**

Glucagon

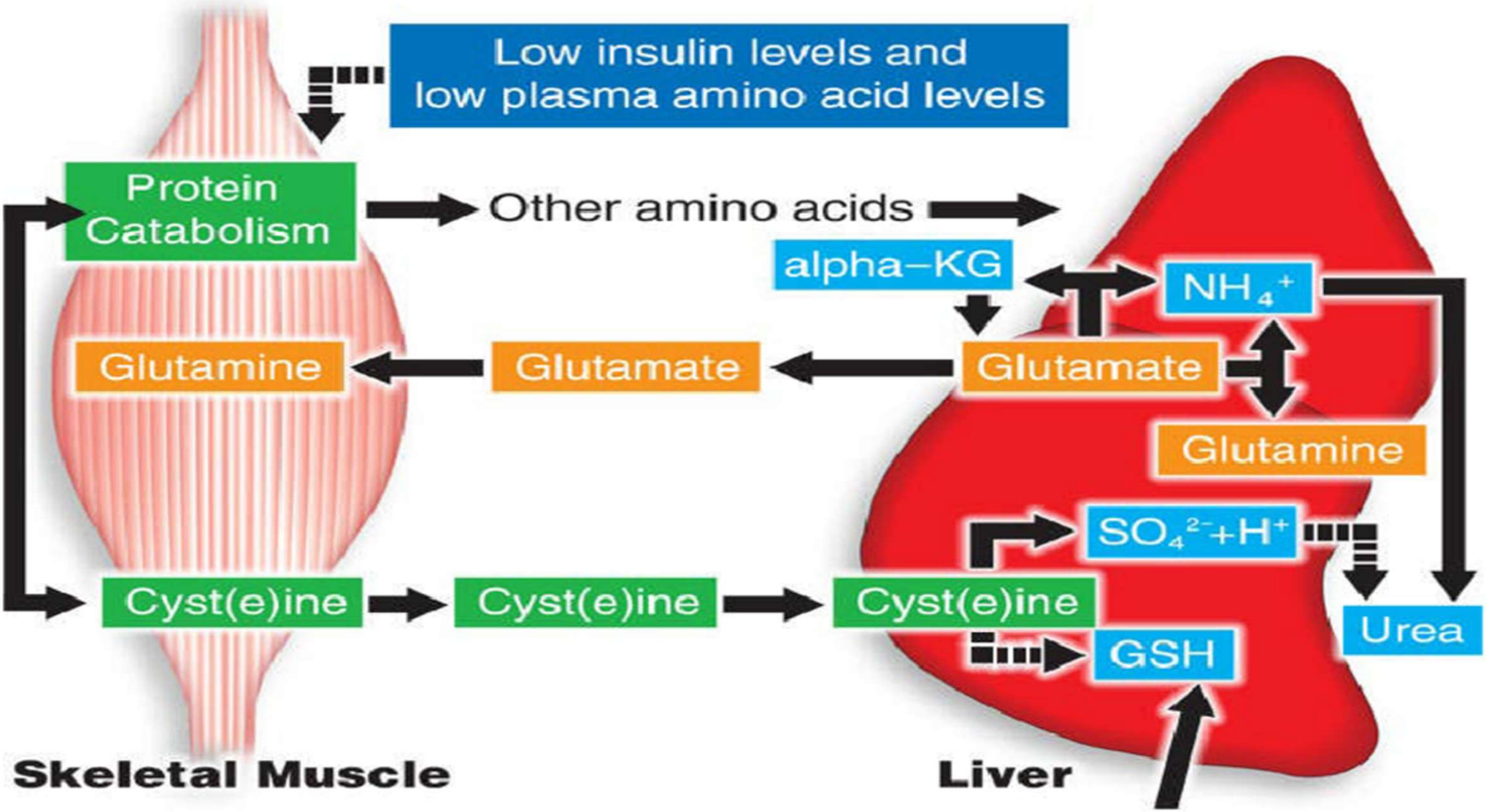
- \+ Stimulates **protein breakdown**
- → Enhances **amino acid uptake** by liver

Growth Hormone

- \+ Increases **protein synthesis**
- ⇄ Works via **IGF-1** in muscle

Cortisol

- \+ Promotes **protein breakdown**
- → Increases **gluconeogenesis**


Low insulin levels and
low plasma amino acid levels
Protein
Catabolism
Other amino acids
alpha–KG
NH_4^+
Glutamine
Glutamate
Glutamate
Glutamine
$SO_4^{2-}+H^+$
Cyst(e)ine
Cyst(e)ine
Cyst(e)ine
Urea
GSH
Skeletal Muscle
Liver

Clinical Significance

Phenylketonuria (PKU)

- **Deficiency:** Phenylalanine hydroxylase
- **Symptoms:** Neurological damage, seizures
- **Treatment:** Low phenylalanine diet

Urea Cycle Disorders

- **Deficiency:** CPS1, OTC, ASS, ASL, ARG1
- **Symptoms:** Hyperammonemia, coma
- **Treatment:** Protein restriction, ammonia scavengers

Muscle Wasting

- **Causes:** Sepsis, trauma, cancer
- **Symptoms:** Weakness, weight loss
- **Treatment:** Nutritional support, anabolic agents

Albinism

- **Deficiency:** Tyrosinase enzyme
- **Symptoms:** Lack of melanin pigment
- **Management:** UV protection, visual aids


Thank
you