2024
SUMMARY

METABOLISM

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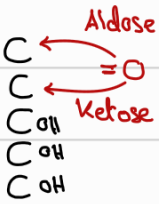
ARKAN ACADEMY

Carbohydrates

Isomers :
- Constitutional isomers : glycose - fructose; Aldose - Ketose
- Stereoisomers → Enantiomers: all OH (L, D isomers)
  - Diastereomers: 1 or more OH (Galactose-Mannose)
  - Epimer: 1 OH (Glucose - Mannose)
- Anomer → OH of anomeric carbon: α → down, β → up

Sugars
- (3C) Glyceraldehyde
- (4C) Erythrose
- (5C) Ribose
- (6C) Glucose (3), Galactose (3,4), Mannose (3,2) — aldose
- (6C) Fructose — Ketose
- (7C) Sedoheptulose
- (9C) Neuraminic acid



Disaccharides
- Maltose (homodimer of glucose)
- Lactose (Galactose - Glucose)

Glycosidase → Break glycosidic bond between sugars

- Examples: Isomaltase (α 1-6), Maltase (α 1-4), Lactase (β 1-4), Sucase (α 1-2), Trehalase (α 1-1)
- Amylase (α 1-4) → Saliva (stops by gastric acidity) and Pancreas
  - Break down starch into small units (not monosaccharides)

Sucrase Isomaltase complex → In the apical surface of intestinal cells

- 1 polypeptide → 2 subunits (Maltase + other glycosidase)
- It can be defecient due to: Genetic mutation, intestinal diseases (celiac and Crohn's) Malnutrition, drugs, diarrhea

☆ Lactase : highest activity in the first month and decreases until age (5-7) years

☆ Absorption of sugars : 1) Cotransport (SGLT) → Secondary active transport with Na^+ → Apical of intestinal, Kidney tubules

2) Na-independent facilitated diffusion (GLUT)
- Down gradeint, Bidirectional, Apical + Basal
- GLUT 1 : Barriers GLUT 2 : Pancreas (Glucose, Galactose, fructose) GLUT 3 : CNS
- GLUT 4 : Insulin sensitive GLUT 5 : Sperms (fructose) GLUT 7 : ER

☆ Metabolic regulation :
- Signals within the cell → Rapid
- Intercellular → Slow, long range
  1) Synaptic : Paracrine (NT) 2) Endocrine : via blood (hormones)
  3) Direct contact : Gap junction

Glycolysis ⇝ Most universal pathway, anaerobic (with or without O_2)

Glucose
- non specific, high affinity → Hexokinase (most tissues)
- specific, low affinity → Glucokinase (Liver)

⊖ ATP

Glucose 6-P
- Trap Glucose

Phosphoglucose Isomerase

Fructose 6-P

⊖ ATP — Phosphofructokinase (PFK) — Rate limiting, Committed step
- activated by AMP and fructose 2,6 bisphosphate

Fructose 1,6-Bisphosphate

aldolase

DHAP ⇌ G3P (Triose phosphate isomerase)

G3P + P_i + ⊕ NADH (G3P DH)

1,3 bisphosphoglycerate

Phosphoglycerate Kinase + ⊕ ATP

3-phosphoglycerate

Phosphoglycerate Mutase

2-Phosphoglycerate

Enolase — form a double bond

Phosphoenolpyruvate

Pyruvate Kinase + ⊕ ATP

Pyruvate

Net: 2 ATP, 2 NADH

anaerobic ← Pyruvate → aerobic

(Recycle NAD^+) Fermentation — Pyruvate oxidation, TCA...

1) Alcohol fermentation: Pyruvate ⇝ acetaldehyde ⇝ ethanol

2) Lactic acid fermentation: Pyruvate ⇝ lactate (by LDH)
- lactic acidosis

☆ RBC shunt: step 7 undergo an alternative path way

1,3-bisphosphoglycerate —mutase→ 2,3-bisphosphoglycerate ⟶ 3-phosphoglycerate
- bind deoxyhemoglobin ⇝ ↑ efficiency of gas exchange

Gluconeogenesis
- Source: non-carbohydrate
- Fasting state → Liver and kidney

Pyruvate + CO_2 (⊖ ATP, Carboxylase (with biotin)) → OAA
- bind
- inhibited by acetyl CoA ⇝

OAA → Malate (mitochondria) → OAA (Cytosol)

OAA + ⊖ GTP (PEP carboxykinase) → PEP

PEP ⋮

Fructose 1,6 bisphosphate
- inhibited by AMP and fructose 2,6 bisphosphate ⇝

Fructose 1,6 bisphosphate phosphatase

Fructose 6-phosphate

Glucose 6-phosphate

Glucose 6-phosphatase (ER)

Glucose
- Transported by GLUT 7

Net: Consume 4 ATP, 2 NADH

☆ At low glucose level ⇝ Hexokinase is active, Glucokinase is inactive (sequestered in the nucleus bound GKPP)
when glucose increases ⇝ Glucokinase became active
when fructose 6-phosphate ⇝ Glucokinase become inactive

☆ PFK-1 ⇝ inhibited by ATP, Citrate and Protons

☆ Pyruvate kinase ⇝ inhibited by ATP and alanine / activated by fructose 1,6-bisphosphate (feed forward activation)

☆ Insulin activates glycolysis, inhibits gluconeogenesis

☆ Glucagon inhibits glycolysis, activate gluconeogenesis
↳ They regulate glycolysis by affecting pyruvate kinase and the bifunctional enzyme

☆ Pyruvate kinase deficiency ⇝ decrease ATP synthesis
↳ ATP deficiency cause decrease Na^+/K^+ pump activity ⇝ decrease flexibility of RBC shape causing hydrolytic anemia and premature death of RBCs

☆ Inorganic inhibitors :
1) Fluoride ⇝ toothpaste which inhibits bacterial enolase
2) Pentavalent arsenic (arsenate): inhibits GA3P DH
3) Trivalent arsenic (arsenite): Bind SH- of lipoyl of Pyruvate dehydrogenase and αkG DH
↳ Arsenic poisoning ⇝ cause neurologic disturbances

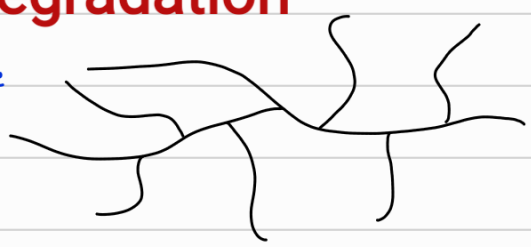
☆ In fasting state: Glycogen (rapid response, limited amount) and Gluconeogenesis (slow)
↳ Muscles > Liver > Extracellar fluid

Glycogen

↳ Homopolysaccharide, extesively branched (branch each 10 residues), α1-4 and α1-6 bonds → branch

Degradation

☆ start on the non reducing ends



☆ Glycogen phosphorylase

Glucose ⇝ Glucose 1-P ⇝ Glucose 6-P → Liver Glucose / muscle Remain

Glycogenesis

☆ Glucose 6-P → Glucose 1-P → UDP-Glucose
Phosphoglycomutase / UDP-glucose pyrophosphorylase

☆ Glycogen synthase: add UDP-glucose to primer

☆ 4:6-transferase ⇝ Branching enzyme (Glycogen fragment → Glycogenin)

2 ATP (UTP) are used per UDP-glucose

☆ Limit dextrin: a strech of sugars befor the branch, stops degradation

☆ Debranching enzyme ⇝ break α 1-6 bond

☆ lysosomal degradation: by α 1-4 glucosidase (acid maltase)

↳ deficiency: Type II Pompe disease

Cardiomegaly and heart failure

☆ Type Ia von Gierke disease

↳ Glucose 6-phosphatase ↓

☆ Type Ib von Gierke disease

↳ Glucose 6-phosphate translocase ↓

Hepatomegaly, Hypoglycemia, delayed Puberty, Growth retardation

Liver, kidney, intestine

☆ McArdle syndrome

↳ ↓ Glycogen phosphorylase

only muscles

Weakness of muscles

No increase in lactate

☆ feeding state: insulin, ↑ Glycogen synthesis

↑ phosphodiesterase

↑ Phosphatase

which activates glycogen synthase and inhibits glycogen phosphorylase

☆ fasting state: glucagon, ↑ degradation

↑ glycogen phosphorylase kinase

↳ phosphorylase b ⇝ a

☆ Glucose 6-phosphate

↳ activate synthase

↳ inhibits phosphorylase

☆ Glucose (Liver) ⇝ inhibit phosphorylase

☆ Ca^{+2}, Calmodulin, AMP (muscle) ⇝ activate Phosphorylase

↓ PKC

↓ Calmodulin dependent Protein Kinase

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