Gluconeogenesis

Synthesis of glucose from non carbohydrate precursors is called gluconeogenesis (synthesis of new glucose)

Precursors :

(1) **Lactate** :⇒ It generated from pyruvate in glycolysis. The lactate transfered to liver by "CORI's Cycle" and is converted to glucose

(2) **Glycerol** :⇒ It form in adipose tissue by hydrolysis of triacylglycerol. The generated glycerol Cannot utilised by adipose tissue due to poor content of Glycerol kinase enzyme. so it is delivered to liver where it Convert in glucose.

(3) **Glucogenic Amino acid**: The Carbon Skeleton of glucogenic amino acid are converted to pyruvate which converted to glucose.

(4) Intermediate of TCA cycle

Location :⇒ Gluconeogenesis occurs mainly in cytosol.

liver is the main tissue for gluconeogenesis.

Characteristic of gluconeogenesis :⇒ ⇒ It involve glycolysis TCA cycle and some special reaction.

→ Glycolysis & Gluconeogenesis Share the same path way but in opposite direction

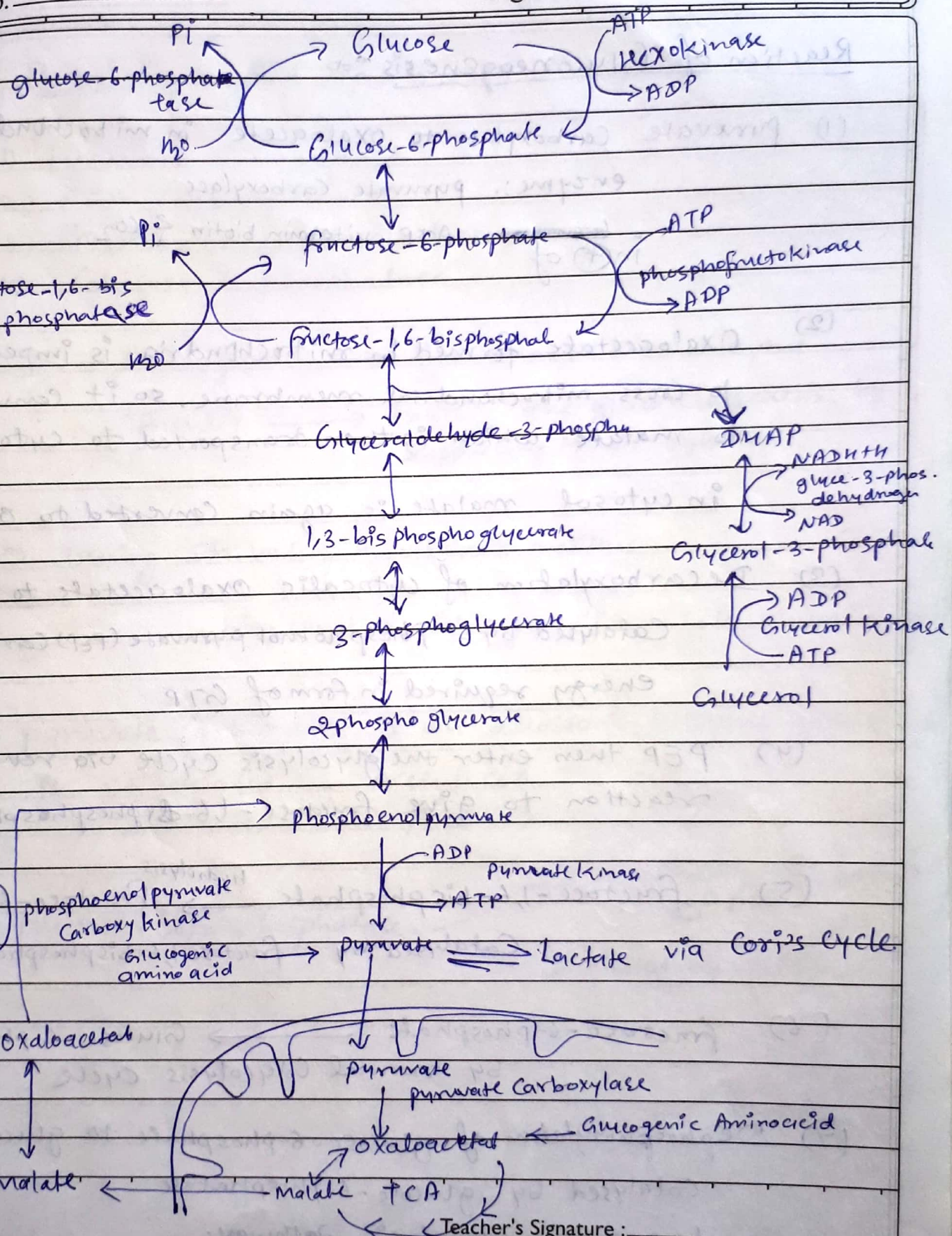
⇒ Special reaction are catalysed by

(a) pyruvate carboxylase

(b) Phosphoenol pyruvate Carboxykinase

(c) fructose 1-6,-bis phosphatase

(d) Glucose-6-phosphatase



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Reaction of Gluconeogenesis :=>

(1) Pyruvate Carboxylate to Oxaloacete in mitochondria.

enzyme:. pyruvate Carboxylase

: ATP, vitamin biotin & CO_2

in ⊕ of

(2) Oxaloacetate formed in mitochondria is impermeable to cross mitochondrial membrane. so it converted to malate which is then transported to cytosol.

in cytosol malate is again converted to Oxaloacetate

(3) Decarboxylation of cytosolic Oxaloacetate to PEP

Catalysed by : Phosphoenol pyruvate (PEP) Carboxykinase

energy required in form of GTP

(4) PEP then enter the glycolysis cycle via reverse reaction to give fructose-1,6-diphosphosphate

(5) fructose-1,6-bisphosphate $\xrightarrow{\text{hydrolysis}}$ fructose-6-phospha

Catalysed by fructose-1,6-bisphosphatase

(6) fructose-6-phosphate ⟶ Glucose-6-phosphate

by normal Glycolysis cycle

(7) Dephosphorylation of glucose-6-phosphate to glucose

Catalysed by glucose-6-phosphatase

bypass the Glycolysis pathway.

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Regulation:- Reg by 4 key enzymes.

(1) Pyruvate Carboxylase
(2) PEP Carboxykinase
(3) Fructose-1,6-bisphosphatase
(4) Glucose-6-phosphatase

⇒ Glucagon ⟶ Stimulate these enzyme
Insulin ⟶ inhibit the gluconeogenesis by suppresing their synthesis.

⇒ During Starvation & diabetes mellitus
↓
High level of Glucagon - stimulate gluconeogenesis

⇒ pyruvate Carboxylase is an allosteric enzyme which is stimulated by Acetyl-CoA
Inhibited by ADP

⇒ fructose-1,6-bisphosphatase → Allosterically stimulated by CAMP
→ Inhibited by AMD

Significance of Gluconeogenesis

(1) Maintain blood glucose level when Carbohydrate is not available in diet.

(2) During long starvation, hepatic glycogen storage is totally depleted.

So glucose is continuous supplied by gluconeogenesis to brain, Lens, Cornia, kidney medula. They need continuous supply of glucose as source of energy.

(3) It is used to clear the product of the metabolism of other tissue from the blood.

such as → Blood Lactate produced by muscle & erythrocyte

Blood → Glycerol produced by adipose tissue

Blood → Propionyl-CoA produced by oxidation of odd carbon number fatty acid