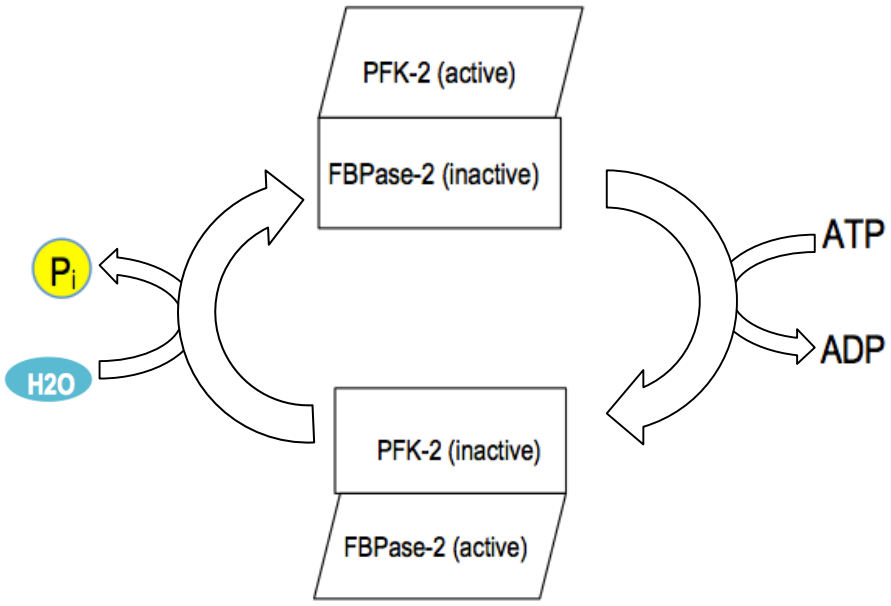
CONCEPT: METABOLIC REGULATION

- Phosphofructokinase-1 (PFK-1) – catalyzes the commitment step of glycolysis
    - □ Has allosteric regulatory sites that bind ATP; high [ATP] lowers enzyme activity
    - □ Citrate is transported out into cytoplasm for biosynthesis, and high concentrations will inhibit PFK-1
    - □ ADP and AMP stimulate the enzyme's activity
    - □ Fructose 2,6-bisphosphate is an allosteric activator, and the most important regulator of PFK-1
        - PFK-1 is considerably less active without fructose 2,6-bisphosphate
        - Fructose 2,6-bisphosphate is effective at extremely small concentrations (~1μM)
        - Fructose 2,6-bisphosphate inhibits fructose 1,6-bisphosphatase, PFK-1's gluconeogenic counterpart
        - AMP also inhibits fructose 1,6-bisphosphatase, and therefore inhibits gluconeogenesis
- Phosphofructokinase-2 (PFK-2) – generates fructose 2,6-bisphosphate to regulate the action of PFK-1
    - □ Insulin causes phosphate group to be removed from enzyme, activates PFK2
    - □ Glucagon leads to phosphorylation of enzyme, activating fructose bisphosphatase 2
    - □ Fructose 2,6-bisphosphate is broken down by fructose bisphosphatase 2; part of same protein as PFK-2
    - □ Phosphoprotein phosphatase dephosphorylates PFK-2; stimulated by xylulose 5-phosphate

INSULIN GLUCAGON



- Pyruvate kinase – last enzyme of glycolysis; only in the liver does glucagon cause PKA to phosphorylate and inactivate it
    - □ Stimulated by fructose 1,6-bisphosphate, an upstream glycolytic substrate
    - □ Inhibited by ATP, acetyl-CoA, and long-chain fatty acids (also alanine, which is derived from pyruvate)
- Pyruvate carboxylase is activated by acetyl-CoA

CONCEPT: METABOLIC REGULATION