Regulation and Inhibition of Pathways

aerobic conditions

Promotes complete catabolism (metabolic breakdown) of glucose, via glycolysis, TCA cycle, and oxidate phosphorylation.

anaerobic conditions

Cannot enter TCA cycle. Must regenerate NAD+ after glycolysis. Pyruvate converted to lactate (all organisms) or ethanol (yeast and some microorganisms).

high [glucose-6-P]

inhibits hexokinase (indicates that there is no need to further convert glucose into glucose-6-P)

high [ATP] (note: high [ADP] or [AMP] have opposite effects**)**

Indicates a state of excess energy. Stop catabolism (metabolic breakdown) of glucose and intermediates, promote formation of glucose to store energy.

- Stops glycolysis, TCA cycle by **inhibiting** the following enzymes:
  - P-fructokinase
  - pyruvate oxidase (takes a very high [ATP])
  - citrate synthase (takes a very high [ATP])
  - isocitrate dehydrogenase
  - v. high [ATP] - pyruvate decarboxylase

- Promotes gluconeogenesis (formation of glucose) by **activating** the following enzymes and/or pathways:
  - glyoxylate cycle (only in microorganisms)—by inhibiting isocitrate dehydrogenase (see above). In this cycle, acetate or acetyl CoA can be converted into glucose.
  - Fructose-1,6-diP Phosphatase

high [Acetyl CoA]

Indicates that more Acetyl CoA is available than is being metabolized via the TCA cycle.

- Promotes gluconeogenesis (formation of glucose) to store excess energy, by activating the following enzymes:
  - pyruvate carboxylase
  - PEP carboxykinase

Regulation and Inhibition of Pathways

epinephrine

Hormone released during "flight or fight response"? need free energy rapidly. Thus promotes breakdown of glycogen into glucose via a regulatory pathway described in class. The end result is that it:

- Induces glycogen phosphorylase
- Inhibits glycogen synthase

arsenite

Reacts with dimercapto compounds (like Lipoic Acid). Thus, blocks:

- pyruvate oxidase particle
- α-ketoglutarate oxidase particle.

arsenate

Analog of phosphate. Incorporated by glyceraldehydes-3-P dehydrogenase in glycolysis. Incorporation leads to hydrolysis: generate 3-P-glycerate without ATP generation. Makes glycolysis reaction net no ATP production. Thus, under anaerobic conditions: no energy from glycolysis.

malonate (a.k.a. malonic acid)

Competitive inhibitor of succinic dehydrogenase. Blocks conversion between succinate and fumarate in the TCA cycle.