Principles of Biosynthesis

- Anabolism (= biosynthesis)
  - Creation of more complex molecules from simpler ones, but requires energy input
  - Carefully balanced with catabolic processes
  - Energy required in terms of ATP is enormous

Principles of Biosynthesis (cont.)

- Biosynthesis is shaped by several guiding principles:
  - All macromolecules are derived from about 30 small precursors
  - Many of the same enzymes used in both catabolism and anabolism
  - End product regulation is generally more important in anabolic pathways

Principles of Biosynthesis (cont.)

- To be efficient, anabolic pathways must operate irreversibly and are usually coupled with the breakdown of ATP
- In eukaryotes, compartmentation permits different pathways to operate simultaneously and independently
- Anabolic and catabolic pathways typically use different co-factors, for example:
  - Catabolism produces NADH
  - NADPH used as electron donor for anabolism

Principles of Biosynthesis (cont.)

- Generation of precursor metabolites is critical step in anabolism
- Carbon skeletons are used as starting substrates for biosynthetic pathways
  - Examples are intermediates of the central metabolic pathways
  - Most are used for the biosynthesis of amino acids
**Photosynthetic CO₂ Fixation**

- Most microbes can incorporate, or fix, CO₂ via anaplerotic or other pathways
- Only autotrophs use CO₂ as a sole carbon source and, therefore, utilize one of three different reductive pathways to do so
- Energy for these pathways comes from photosynthesis or lithotrophy

**Autotrophic CO₂ Fixation (cont.)**

- **Calvin Cycle** (reductive pentose phosphate cycle)
  - Present in photosynthetic eukaryotes and most photosynthetic prokaryotes
  - Absent in Archaea, some prokaryotic obligate anaerobes and microaerophiles
  - Occurs in:
    - Chloroplast stroma (eukaryotes)
    - Carboxysomes (prokaryotes)

**Autotrophic CO₂ Fixation (cont.)**

- **Three phases**
  - Carboxylation
    - CO₂ is incorporated into ribulose 1,5-bisphosphate (RuBP; 5 carbon molecule) to form two molecules of 3-phosphoglycerate (PGA; 3 carbon molecules)
    - Catalyzed by the enzyme ribulose-1,5-bisphosphate carboxylase
  - Reduction Phase
    - PGA is reduced to glyceraldehyde 3-phosphate
    - Requires one molecule of ATP and one molecule of NADPH for this reduction process to occur
Autotrophic CO₂ Fixation (cont.)

- Regeneration Phase
  - RuBP is regenerated via a series of reactions that resemble the pentose phosphate pathway
  - Also generates a number of different carbohydrate structures that can be used elsewhere in the cell
- Total energy expenditure (provided by photosynthesis or chemotrophy):
  - 2 ATP molecules
  - 3 NADPH molecules

Gluconeogenesis

- Non-photosynthetic microbes synthesize sugars from reduced organic molecules
- Synthesis of glucose using noncarbohydrate precursors is termed **gluconeogenesis**
- Gluconeogenic pathway is remarkably similar to reverse glycolysis

Gluconeogenesis (cont.)

- Gluconeogenic pathway
  - Shares seven (7) enzymes with glycolysis
  - Three steps are irreversible
  - Some sugars are synthesized as nucleotide diphosphates which play a role in polysaccharide formation
Anaplerotic Reactions

◆ The demand for intermediates of pathways can lead to a depletion of these compounds, thus disrupting the particular metabolic process, e.g., use of oxaloacetate from the TCA cycle to make amino acids.
◆ Microbes have developed reactions, termed anaplerotic reactions, to replace these lost intermediates.

Anaplerotic Reactions (cont.)

◆ Most microbes will replace TCA cycle intermediates by CO₂ fixation - NOT the same as the Calvin Cycle or other pathways that fix CO₂ to produce carbohydrates.
◆ CO₂ is added to another compound that forms an intermediate.
◆ Functions as a replacement process, not for cellular growth.
◆ Maintains the operation of the TCA cycle.

Anaplerotic Reactions (cont.)

◆ Some microbes use the glyoxylate pathway to maintain the operation of the TCA cycle as well as to grow on two-carbon sources (e.g., acetate).
◆ Essentially a modified TCA cycle.
◆ Two key enzymes:
  > Isocitrate lyase
  > Malate synthase
◆ Pathway is essential for the survival of some pathogenic microbes in vivo.

The Glyoxylate Cycle

Fig. 12.24