

Study Guide – Lehninger Principles 5th Edition

Chapter Sixteen

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Homework: 3-5,9,10,14,19,23. **16.1 Production of Acetyl-CoA.** As with Glycolysis, you should really know “everything” about the reactions of the Citric Acid Cycle (section 2) and the mechanism of the Pyruvate D.H. Complex (this section). So you should be able to draw structures of reactants and products, know enzyme names, and be able to supply correct cofactors for all reactions involved.

To focus on the Pyruvate DH Complex, (and the parallel α -KGDH Complex), it is important to always have “*five things under the arrow*” namely CoA, NAD⁺, FAD, TPP, and lipoamide. Also know the names and actions of the three component enzymes, and the structures and actions of lipoamide and TPP as given in class.

16.2 Reactions of the Citric Acid Cycle. Look at Fig 16-7. We will begin with Succinate, at “7:00” on the cycle. The CAC takes place in the mitochondrial matrix, but Succinate DH is an integral membrane protein with Iron Sulfur Clusters. The reactions from Succ to OAA are reversible and can function in parallel with the other half of the pathway (Fig 16-14). The ΔG° for conversion of L-Malate to OAA is +29.7 kJ/mol, and the ΔG° for Citrate Synthase is –32.2 kJ/mol. With the α -KGDH Complex (–33.5 kJ/mol) these are the largest standard free energy changes in the cycle, and they can lead to a deficiency of OAA which must be remedied by “anaplerotic reactions” (631ff). Remember Pyruvate Carboxylase (Fig 16-16) is also important in Gluconeogenesis (Fig 14-18). Please include cis-Aconitate as an intermediate of the CAC (square brackets as in Fig 16-7 are not necessary). Aconitase also contains an iron-sulfur (Fig 16-10). The mechanism of ICDH (Fig 16-11) includes electron-sink driven decarboxylation. α -KGDH has the same mechanism as Pyruvate DH Complex. Succinyl CoA Synthetase catalyzes the only “substrate level phosphorylation” in the pathway. Know what this means (see p. 537). Read the nomenclature box (Box 16-2 page 627) and know the distinctions (i.e. Synthase versus Synthetase). Understand why the symmetry of Citric Acid was confusing to early researchers (Box 16-3) which led to the name “TCA” or Tricarboxylic Acid Cycle. Know that the overall yield of ATP per Glucose is 30 or 32 (Table 16-1 p. 630).

16.3 Regulation of the Citric Acid Cycle. Study the summary of regulation in Fig 16-18. The regulation occurs at the “irreversible” (the book says “exergonic”) steps, where CO₂ is lost or, in the case of Citrate Synthase, a high energy thioester bond is broken. Enzymes are inhibited either by their immediate products or by their eventual products. With an oxidative catabolic pathway it’s not surprising that ATP and NADH figure prominently among the inhibitors. Low energy charge (represented either by AMP or ADP) is a stimulant.

16.4 The Glyoxylate Cycle. Not much time for this – but know that 1) it is *not* part of human metabolism, but restricted to plants and micro-organisms and 2) it allows net conversion of Acetyl CoA to glucose. Without it, “sugar can make you fat, but fat can’t make you sweet!”