BC 368- Biochemistry of the Cell II
Problem Set #10 Solutions

1. Platelets are specialized disk-shaped cells in the bloodstream that are involved in the formation of blood clots. They play an important role in heart attacks, strokes, and peripheral vascular disease. Platelets act as tiny building blocks to form the basis of a clot to stop bleeding from cuts or injuries. Platelets can detect a disruption in the lining of a blood vessel and react to build a wall to stop bleeding.

   In cardiovascular disease, abnormal clotting can result in heart attacks or stroke. Blood vessels injured by smoking, cholesterol, or high blood pressure develop cholesterol-rich build-ups (plaques) that line the blood vessel; these plaques can rupture and cause the platelets to form a clot. Even though no bleeding is occurring, platelets sense the plaque rupture and are confused, thinking that an injury has taken place that will cause bleeding. Instead of sealing the vessel to prevent bleeding as would occur with a cut, a clot forms in an intact blood vessel, causing a blockage of blood flow.

   a) These fatty acids are incorporated into the platelets instead of arachidonic acid.

   b) The n3 PUFAs disrupt the formation of lipid rafts!

   c) A longer time is needed for clotting, so clotting is inhibited when the omega-3's are incorporated into platelets.

   d) EPA and DHA are incorporated into the membranes of platelets, where they inhibit formation of lipid rafts, which are important for recognition of collagen. Thus, they collagen recognition and subsequent formation of thrombi are inhibitied.

   e) In men, only the EPA treatment significantly reduced platelet aggregation compared with placebo (P = 0.005) and women (P = 0.011). In contrast, in women, only the DHA treatment reduced platelet aggregation compared with placebo (P = 0.001) and men (P = 0.017). Sex hormone levels appear to influence n3 PUFA uptake and metabolism, and men are more likely to benefit from supplementation with EPA, whereas women are more responsive to DHA.

4. The data suggest that three enzymes- pyruvate dehydrogenase, α-ketoglutarate dehydrogenase, and the branched-chain α -ketoacid dehydrogenase- are deficient. Most likely the common E_3 component of these enzymes is defective. This diagnosis could be tested by purifying these three enzymes and assaying their ability to regenerate lipoamide. Note that thiamine deficiency is not a defect, and so this would not be a viable answer.

6. a) When glycogen stores are depleted, the body's proteins must be degraded to make glucose for the brain. The resulting amino acids are deaminated and the nitrogen excreted as urea. The carbon skeletons undergo gluconeogenesis.

   b) The brain adapts to the use of ketone bodies after about a week. Lipid stores can thus replace protein degradation to fuel the brain. When all glycogen and lipid stores are gone, the only available source of energy is protein. Again, the resulting amino acids are deaminated and the nitrogen excreted as urea.