

Question 1

TCA cycle

In diabetes mellitus, the body's ability to use glucose as a primary source of energy is impaired due to insufficient insulin production (Type 1 diabetes) or insulin resistance (Type 2 diabetes). As a result, the body begins to use alternative sources of energy to meet its metabolic needs. When glucose and fat stores are insufficient, the body starts breaking down muscle proteins into amino acids through proteolysis.

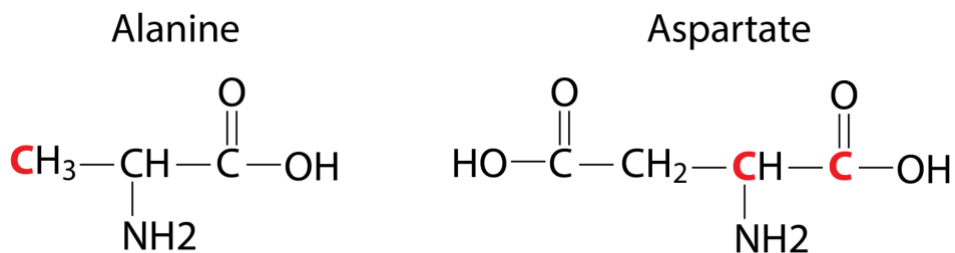


Fig. 2

- a) Imagine that the breakdown of endogenous proteins yields labelled amino acids: Alanine labelled at C3 and Aspartate labelled at C1 and C2 (**Fig. 2**), which then enter the TCA cycle. Where do we find the [^{13}C] label after one TCA cycle? (2 pts)
- b) Fluoroacetic acid is a harmful metabolite. Fluoroacetic acid can disrupt the Krebs cycle. The metabolite of fluoroacetic acid is fluorocitric acid, which is very toxic because it cannot be processed by aconitase in the Krebs cycle (where fluorocitrate takes the place of citrate as the substrate). The enzyme is inhibited and the cycle stops working. Where will you find the [^{13}C] label from Aspartate and Alanine (see **Fig. 2**) in the presence of fluoroacetic acid? (3 pts)
- c) Now imagine that Aspartate is uniformly labelled at all carbon positions. Where do we find the label after two TCA cycles and where after three? (2 pts)

Question 2:

Myocytes (skeletal muscle cells) are specialized in generating ATP as a source of energy for contraction. Slow-twitch muscles (red muscles) provide low tension but are resistant to fatigue. They produce ATP through a relatively slow but steady process of oxidative phosphorylation. Fast-twitch muscles, on the other hand, use glycolysis, can develop greater tension, and do so more quickly. In contrast to slow-twitch muscles, they fatigue more quickly.

- a) A group of students decides to perform an experiment where they would use myocytes belonging to both muscle types in separate cell culture dishes. They will stimulate myocytes to contract to 100 % (maximum capacity). The culture medium in which myocytes grow contain the following -[^{13}C] labelled molecule: Fatty acid (17 C atoms) labelled at C2, C10 and C17 (**Figure 5**). Which myocytes will contain the label and in which molecules (assume only one TCA cycle is allowed) (5 pts)?

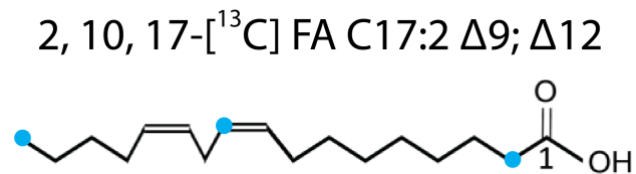


Fig. 5