**Questions for Practical 2: Cancer Metabolism**

*Questions for the healthy cell culture model (FBA\_normal.mlx)*

* **Section 1:**
  + **Question: You might recognize some of the components of the RPMI medium (based on the web links). What is the symbol used for glucose in the model?**

D-Glucose (Dextrose)

EX\_glc(e) – concentration of 11.11

* **Section 2:**
  + **Question: What is the flux through the ATP demand reaction and how does it compare to the maximum of 1000? What does this mean biologically?**

Maximum O2 uptake: 1000mol/min/gDW

Objective Value = 1000, thus, 1000 ATP is produced. Because O2 is constraint to 1000, the maximum of ATP produced is 1000. 1 glucose molecule produces 32 ATPs; however, maximum ATP is capped at 1000.

* **Section 3:**
  + **Question: What is the flux through the ATP demand reaction and how does it compare to the flux in the aerobic case above? What does this mean biologically?**

Input 0 oxygen, and output is 70 ATP’s. This means that during anaerobic respiration (no oxygen) maximum 70 ATPs are produced.

Minimum: 70 ATP’s

* **Section 4:**
  + **Question: Via which reaction is lactic acid produced during respiration? Do you expect more or less production of lactic acid in the anaerobic model?**

Lactic Acid is produced during anaerobic reaction (no oxygen) produces lactic acid (lactate). More production of lactic acid in the anaerobic model.

* + **Question: What is the name of the reaction producing lactic acid from pyruvate?**

Anaerobic Respiration

* + **Question: What is the flux through this reaction in the aerobic model? And in the anaerobic model?**

Diagram

Description automatically generated

Flux for Aerobic = 29.85

Diagram

Description automatically generated

Flux for Anaerobic = -63.12

* The square is the reaction, so it is the weight of the arrows
* Negative sign means the direction (pyruvate to lactate is -, lactate to pyruvate is +)
  + Question: Did you expect this difference from a biological perspective? Briefly explain.

Yes, because to produce lactate from pyruvate you need to break the bonds so energy is needed, therefore the negative flux.

*Questions for the cancer cell culture model (FBA\_cancer.mlx)*

* Section 1:
  + Question: Inspect the code above. Explain in your own words what we did to create a cancer specific model.
* Section 2:
  + **Question: inspect the flux through ATP demand. How does it compare to the healthy (i.e. non-cancer) model? (*aerobic)***

Input of oxygen = 1000, but only 988.09 ATP produced. In cancer cells, ATP is produced via Glycolysis, O2 is not such a vital requirement – but still important. If we input oxygen = 500, we get 614 ATP.

Glycolysis = Anaerobic (no oxygen)

Produces less ATP in cancer cell than in healthy cell (1000).

* + **Question: inspect the flux through ATP demand. How does it compare to the healthy (i.e. non-cancer) model? *(anaerobic)***

0 oxygen = 67 ATP. Normal Healthy cells produces 70 ATP. Meaning, healthy and cancer cells operate similarly under no oxygen environment.

* **Section 3:**
  + **Question: Does the reaction converting lactic acid and pyruvate have a positive or negative flux in the cancer model? Does it differ between aerobic and anaerobic conditions?**

Pyruvate to lactate = negative

Lactate to pyruvate = positive

Cancer = both aerobic and anaerobic are negative because always pyruvate to lactate (doesn’t go through the OXPHOS pathway)

* + **Question: Is the glycolysis reaction more or less active in the cancer model compared to the healthy model?**

Glycolysis is more active in the cancer model. Although glycolysis is less efficient than oxidative phosphorylation in the net yield of adenosine triphosphate (ATP), cancer cells adapt to this mathematical disadvantage by increased glucose up-take, which in turn facilitates a higher rate of glycolysis.

* + **Question: Do the results align with what is known of aerobic cancer metabolism? Briefly explain.**