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Scientific Literacy 2

Inorganic phosphate (Pi) is an essential nutrient of which phospholipids rely on in order to activate certain metabolic pathways which allow them to biosynthesize as mentioned earlier. Pi appears to have a significantly more complex intracellular method of metabolizing within the body. A recent study by Xu, et. al, *A phosphate-sensing organelle regulates phosphate and tissue homeostasis*, investigated the process in which Pi affects the amount and size of multilamellar organelles termed PXo bodies[1]. PXo bodies are newly created phospholipids which serve a major role in the endomembrane system. These organelles are acidic and are very similar to alpha fold-predicted structures for the human orthologue XPR1. Orthologues are homologous genes which retain equivalent functions within different organisms[2]. The endomembrane system relies on the transportation of Golgi proteins and glycosylation for continued propagation and maintenance. Glycosylation is the process of carbohydrates attaching to the backbones of proteins and lipids which alters the structure allowing for these macromolecules to serve different functions.[3]

Drosophila melanogaster, more commonly known as fruit flies, were the experimental subjects of this experiment. These fruit flies had their digestive epithelium studied after being fed normal food and PFA food. Pi is absorbed within the cells in order to process and maintain homeostasis and is easily absorbed from normal food. PFA food, PFA standing for inorganic pyrophosphate analogue, effectively inhibits the cellular uptake of Pi. In order to examine the results of this experiment, researchers utilized Forster resonance energy transfer (FRET) to measure the cytosolic phosphate levels. If PXo bodies were to have any effect on the levels of Pi within the cytoplasm, FRET would present these changes accordingly.

Choline analogue (propargyl choline/P-Cho) was injected into the intestinal epithelial cells to observe the newly formed phospholipids from the endoplasmic reticulum. Visualization of gene expression is made possible by FLiPPi, fluorescent reporter proteins, which emit light at a specific wavelength[5]. This light signals gene expression and the location of where these genes are present. Figure 3. E of the study is a colorized visualization of enterocytes expressing FLiPPi from PXo bodies. Figure 3. I displays a quantification of the enterocytes expressing FLiPPi with PXo-HA for 7 days. This figure shows a higher average FRET ratio (.9-1.3 μm) compared to the control (.9-1.2 μm). This leads to the assumption that PXo mediates Pi transport from the cytosol into PCo bodies due to its close proximity to the PXo bodies membranes. FLiPPi was expressed within the cytosol but not inside PXo bodies. This is supported by increased FRET ratios (phosphate levels) when the living digestive tissues of the fruit flies fed PFA showed increased FRET ratios. MSF10, a gene that encodes for transporter proteins[4], knockdown also increases FRET ratios which is logical as this gene mediates Pi uptake.

The formation of PXo bodies relies on the availability of Pi due to PXo bodies being sensitive to Pi availability. Figure 4. H displays the average PXo body number per cell of 4 substrate groups; normal, Pi, PFA, and Sodium sulfate (Si). PFA showed the lowest average PXo body number per cell with 1-4 PXo bodies/cell. The normal group yielded 3-8 bodies/cell, Pi group yielded 6-9 bodies/cell, and Si yielded 5-6 bodies/cell. Figure 4. I displays the relative PXo body size of the aforementioned 4 groups. The relative body size of the PFA group (.546) was significantly lower than all other groups (normal, 1, Pi, 1.11, and Si, 1.022). The PFA group remained consistently the lowest compared to all other groups while the Pi group remained the highest. The credibility of the results are supported by the facts that PFA inhibits Pi uptake while increased Pi within the cell allows the PXo to thrive; growing in size and number.

PXo transports cytosolic Pi into PXo bodies which is essential as it restricts/regulates the amount of phosphate within the cytosol. If phosphate levels were to drop within the cytoplasm, the amount/types of phospholipids found within PXo bodies would drop. Figure 5. D and E display the percentage of phospholipids within a control body and PFA influenced body respectively. The control body had a 90.6% phospholipid composition whereas the PFA PXo body had a 84.2% phospholipid composition. This is a 6.4% decrease which is significant as if there are less phospholipids; it significantly inhibits the homeostasis and metabolism of the cells. Phosphatidic acid is the simplest phospholipid which precedes other more complex phospholipids[6]. If there is not much phosphatidic acid, there will be a decrease in complex phospholipids.

The data collected from the study convinces me that PXo bodies form distinct organelles with their own unique biochemical function within the cell. Inorganic phosphate has shown to play a significant role in cell metabolism as their absence influences the cell's composition and amount of gene expression. PXo bodies store and regulate Pi which serves an essential role for the cell to continue maintaining homeostasis. Without Pi, life would be much harder to maintain as many enzymatic reactions and gene expression would be unable to occur.

References

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