A nurse notices after birth a newborn is blue and cold to the touch. A pulse is present but the newborn has gasping respirations. The nurse applies a respirator until the baby can breathe adequately on its own. What could cause such an issue in a newborn? Respiratory Distress Syndrome or RDS typically occurs when a child is born prematurely [1]. The absence of Pulmonary surfactant is the typical cause of such a syndrome [2]. So how does its absence cause such drastic effects on the newborn's breathing ability? Pulmonary surfactants combine phospholipids and proteins to decrease surface tension where gas exchange occurs [3]. These proteins and phospholipids are secreted on the surface of cells by Alveolar type II cells. Premature newborns have not had the time to develop sufficient quantities of Alveolar type II cells which explains why the premature newborn developed RDS [2]. So what makes these Alveolar type II cells and the lipid-protein complexes they secrete so special?

Alveolar type II cells contain a special organelle that allows them to secrete these lipid-protein complexes. MLBs or Multilamellar bodies are organelles, bound by a membrane, which contains membrane layers like an onion [4]. The key thing that sets these organelles apart is the level of surface area for secretion these membrane layers form. This enables MLBs to have multiple functions in the body from lipid storage to secretion. There are even unilamellar structures in cells, one layer of membrane, usually in the form of vesicles [5]. MLBs are even known to form a part of the lysosomal pathway and can secrete lysosomal enzymes [5]. The organelles may have an origin from our protozoan cousins [6]. Dictyostelium discoideum, a soil amoeba, is able to survive through hunting bacteria. While it is unknown at this moment what they use these cells for in their environment their existence points to a possible origin for these unique organelles.

The ability of the pulmonary surfactant to enable our ability to breathe is made possible by the lipid-protein complexes that make up the surfactant. What enables these unique properties is the inorganic phosphate component of these complex molecules. Inorganic phosphate is used in important cellular processes such as ATP synthesis, formation of nucleic acids, creation of phospholipids, and protein synthesis [7]. It is especially important for our cellular metabolism. Phosphorylation is the first step in glycolysis which is an essential enzymatic process in our metabolism [8]. In addition, it forms a major component of adenosine triphosphate (ATP) which forms the main source of short-term energy in our cells. Inorganic phosphate's role in Phospholipids is what enables the formation of those lipid-protein complex and multilayer membranes in MLBs. The phosphate group in the phospholipid is hydrophilic and forms the extracellular and intracellular facing head while lipids form the hydrophobic tail sandwiched between the two heads [9]. This allows the creation of a barrier against the outside environment allowing for storage and the creation of large surface areas for secretion. Phospholipids are even essential for mitochondrial function and metabolism with mitochondria producing four phospholipid molecules for maintaining homeostasis [10]. Failure to produce these phospholipid molecules in sufficient quantity could cause debilitating mitochondrial disease.

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In the Nature paper "A phosphate-sensing organelle regulates phosphate and tissue homeostasis" the authors examine and attempt to demonstrate separation of Pxo bodies from known organelles. In Figure 2 the PXo bodies are shown to be roundly shaped and are acidic but do not express the Lamp1 lysosome marker, the ManII Golgi marker, or the Dextran endocytic pathway marker. The PXo bodies are lipid-associated and express the P-cho marker for phospholipids. Therefore these bodies are primarily composed of said phospholipids. The PXo bodies also expressed the ConA glycosylation probe so those phospholipids are glycosylated. In Figure 3 we are introduced to fluorescence resonance energy transfer data for Pxo-i protein. When the Pxo-i protein is expressed, levels of inorganic phosphate are regulated down and the yellow fluorescent molecules are visible. When the Pxo-i protein is inhibited through RNA inhibition the levels of inorganic phosphate are not regulated and the inorganic phosphate binds between the blue fluorescent molecules and the yellow fluorescent molecules leaving the blue the only visible molecule. This means that the Pxo-i protein regulates the availability of inorganic phosphate in the cytoplasm through pumping inorganic phosphate outside of the cytoplasm.

In Figure 4 the effect of the presence of inorganic phosphate is tested on the size and number of Pxo bodies in a cell. The photos demonstrate a visible decrease in size when the PFA and Pxo-i inorganic phosphate inhibitor was introduced. More specifically the graph demonstrates that the normal Pxo body has an average diameter of 1 μm and both the PFA and Pxo-i inorganic phosphate inhibitor samples had a diameter under 0.5 μm. With additional inorganic phosphate, the average diameter grew to slightly above 1 μm. For the number of Pxo bodies, the photos showed the expected result that the number of Pxo bodies decreased to nearly zero when the PFA inorganic phosphate inhibitor was introduced. Similar to the size increase the number of Pxo bodies increased visibly in the photos with the introduction of additional inorganic phosphate. More specifically the normal number of Pxo bodies per cell was an average of around 6 with the PFA inhibitor sample around 3 and the increased phosphate around 7. The sodium sulfate control for the inorganic phosphate supplement showed a similar result to the normal sample. So we can conclude from the figure that the size and number of Pxo bodies are dependent on the amount of inorganic phosphate available in the cytoplasm.

In Figure 5 the pie charts demonstrate the ratio of lipids in the normal control Pxo bodies and PFA inhibitor Pxo bodies. In the control sample, the amount of phospholipids was 90.6% of the pie chart while the PFA inhibitor sample dropped down to 84.2% phospholipids. The primary components of both were phosphatidylcholine(PC), phosphatidylethanolamine(PE), and phosphatidylserine(PS). In the control sample, the percentages were 45% PC, 35% PE, and 3% PS while the PFA inhibitor sample had a decreased 39% PC, 35% PE, and increased 4% PS. Phosphatidic acid makes up the precursor molecule for these phospholipid components discussed. The authors of this paper have demonstrated that these Pxo bodies are not directly connected to any existing organelles or cellular pathways. In addition, they have demonstrated

that these organelles have a unique role in inorganic phosphate regulation in the cell. There I can conclude based on this paper that there is sufficient evidence for Pxo bodies forming a new kind of organelle within cells.

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