1. Experiment Title

Structure and Function Relationship of Erythrocyte Band 3.

2. Principal Investigator

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3. Outline of Experiment

Oxygen is essential to most forms of life, but too much oxygen is harmful and can elicit tissue damage. Living creatures, therefore, have a tightly regulated system to deliver the necessary amount of oxygen to specific tissues at the right time. Band 3 (HEM-B3; anion exchanger 1, AE1) mediates the exchange of the cellular HCO_3^- with Cl^- in plasma, which has been known as the "Chloride Shift". Owing to the "Chloride Shift", erythrocytes can discriminate the metabolically active cells from inactive cells and deliver oxygen particularly to metabolically active tissues. Utilizing the synergistic effects of hemoglobin, carbonic anhydrase and the anion exchange activity of band 3, erythrocytes provide an ideal vehicle for delivering oxygen to tissues, depending on their metabolic activity. No excess oxygen is supplied to tissues as far as oxygen is delivered by erythrocytes. Band 3 plays pivotal roles of the oxygen delivering system.

Band 3 consists of 911 amino acids, and its 40-kDa N-terminal domain has a role in maintaining the shape of erythrocytes. The 55-kDa C-terminal half of band 3 penetrates the cell membrane more than 10 times and carries out the HCO_3^-/Cl^- exchange activity. Kinetic studies on anion transport revealed the anion exchange is mediated a one-by-one electroneutral process in both directions, as indicated by the "ping-pong" model. The model suggests that transport is regulated through a single conformational change in band 3. This conformational change leads to the transfer of a single substrate anion across the membrane, and the rates of association and dissociation of the substrate are much faster than the rate of the conformational change that leads to the translocation of the bound anion. Many previous studies have shown that lysine, glutamate, arginine, and histidine residues are essential for anion transport. In particular, His 834 participates in the conformational change between the outward facing and inward facing forms of band 3, which leads to the transfer of a single substrate anion across the membrane. The structural and functional relationship of band 3 has been investigated all over the world for more than 30 years, there is still little known the molecular mechanism of the anion exchanger. It is because we could not get the crystal structure with high resolution.

Objective of this space experiment is to obtain high quality crystals of band 3 protein with resolution of 3 Å or higher, using the microgravity environments of the International Space Station, in order to reveal the structural and functional relationship of erythrocyte band 3. The PCRF (Protein Crystallization Research Facility) of the Japanese Experiment Module "Kibo" will be used for this experiment.

4. Experiment Facility

Protein Crystallization Research Facility (PCRF)