PATHOBIOLOGY OF ERYTHROCYTE BAND 3 DEFICIENCY IN CATTLE

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Pathobiological studies were carried out to elucidate molecular defects underlying the disorders in bovine subjects that exhibited moderate anemia with inherited abnormal shapes of erythrocytes and retarded growth. We analyzed the red cell membranes from the propositi by immunoblotting and demonstrated that the propositus erythrocytes lacked band 3 protein completely. Band 3, the most abundant transmembrane protein, participates in attaching the spectrin-actin network to the plasma membrane through its association with ankirin. Thus, the lack of band 3 causes impaired connection between the membrane skeleton and the plasma membrane and a significant decrease of the contents of major membrane skeletal components. As a consequence of the aberration in membrane organization, the erythrocytes of the propositi showed a great variety of shapes with mechanical instability and decreased deformability. These cells showed severe fragmentation, resulting in a shortened life span, and thus anemia.

Band 3 also functions as an anion transporter mediating rapid Cl^-/HCO_3^- exchange across the plasma membrane. The exchange rate of Cl^- was about 1/40,000 that of the band 3-mediated transport, far less than the Cl^-/HCO_3^- exchange required for effective CO_2 transport and maintaining acid-base balance. Consequently, the propositus blood showed a decrease in the HCO_3^- concentration to ~75% of that in normal cattle, resulting in mind but chronic acidosis (~0.15 pH unit). In addition to moderate anemia, the acid-base disorder could be a cause of the retarded weight gain of the propositi. In the propositi immunoblotting revealed the absence of the renal band 3 isoform involved in HCO_3^- reabsorption and H^+ secretion, which could play some part in this anomaly. However, O_2/CO_2 exchange in propositi appeared to be as effective as in normal cattle, indicating that the role of band 3 in carrying CO_2 is limited.

These results showed that hereditary band 3 deficiency, presumably due to a band 3 gene defect, is the cause of anemia and retarded growth in affected animals. Hence, our study demonstrated that band 3 indeed contributes to mechanical properties of the cells and acid-base homeostasis, but is not essential to survival of these mammals.