

Involvement of Band3 in the efflux of sphingosine 1-phosphate from erythrocytes

Abstract

Sphingosine 1-phosphate (S1P) is a bioactive lipid mediator that is thought to be involved in various diseases. Although the main source of S1P in the plasma is erythrocytes, how S1P is exported from erythrocytes has not been elucidated. When we differentiated K562 cells into erythroblast-like cells with sodium butyrate, we observed that the efflux of S1P was increased without increased expression of previously proposed S1P transporters, while the expression levels of Band3 were increased. Therefore, in this study, we investigated the involvement of Band 3, the most characteristic membranous transporter for erythrocytes, in S1P efflux, using 4,4'-diisothiocyanatodihydrostilbene-2,2'-disulfonic acid, disodium salt (H2DIDS), which is an inhibitor of Band3. First, we treated human washed erythrocytes with H2DIDS and found that H2DIDS decreased the S1P levels in the supernatant, while it increased the cellular S1P contents. Next, when we injected H2DIDS into mice, the plasma S1P level was significantly decreased. Finally, when we overexpressed or suppressed Band3 in K562 cells, S1P efflux was enhanced or decreased, respectively, while the overexpression of Band3 in HEK293 cells did not modulate S1P efflux. These results suggested the possible involvement of Band3 in the transport of S1P, a multi-functional bioactive phospholipid, from erythrocytes.