The highly conserved extracellular peptide, DSYG(893-896), is a critical structure for sodium pump function.

Abstract:

The peptide sequence DSYG(893-896) of the sheep sodium pump alpha 1 subunit is highly conserved among all K(+)‐transporting P‐type ATPases. To obtain information about its function, single mutations were introduced and the mutants were expressed in yeast and analysed for enzymatic activity, ion recognition, and alpha/beta subunit interactions. Mutants of Ser894 or Tyr895 were all active. Conservative phenylalanine and tryptophan mutants of Tyr895 displayed properties that were similar to the properties of the wild-type enzyme. Replacement of the same amino acid by cysteine, however, produced heat-sensitive enzymes, indicating that the aromatic group contributes to the stability of the enzyme. Mutants of the neighbouring Ser894 recognized K(+) with altered apparent affinities. Thus, the Ser894-->Asp mutant displayed a threefold higher apparent affinity for K(+) (EC(50) = 1.4 +/- 0.06 mm) than the wild-type enzyme (EC(50) = 3.8 +/- 0.33 mm). In contrast, the mutant Ser894-->Ile had an almost sixfold lower apparent affinity for K(+) (EC(50) = 21.95 +/- 1.41 mm).

Mutation of Asp893 or Gly896 produced inactive proteins. When an anti-beta 1 subunit immunoglobulin was used to co‐immunoprecipitate the alpha 1 subunit, neither the Gly896-->Arg nor the Gly896-->Ile mutant could be visualized by subsequent probing with an anti-alpha 1 subunit immunoglobulin. On the other hand, co‐immunoprecipitation...
was obtained with the inactive Asp893-->Arg and Asp893-->Glu mutants. Thus, it might be that
Asp893 is involved in enzyme conformational transitions required for ATP hydrolysis and/or ion
translocation. The results obtained here demonstrate the importance of the highly conserved peptide
DSYG(893-896) for the function of alpha/beta heterodimeric P-type ATPases.