論文の内容の要旨

論文題目　Functional analysis of SNP mutations leading to single amino acid substitution in NBCe1

和訳：Na^+-HCO_3^-**共輸送体（**NBCe1**）の単一アミノ酸置換を伴う** SNP **変異体の機能解析**

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The electrogenic Na^+-HCO_3^- cotransporter NBCe1 encoded by *SLC4A4* plays essential roles in the regulation of intracellular/extracellular pH. Homozygous mutations in NBCe1 cause proximal renal tubular acidosis associated with ocular abnormalities. In the present study we tried to perform functional characterization of the 4 nonsynonymous single nucleotide polymorphisms (SNPs), E122G, S356Y, K558R, and N640I in NBCe1A. Functional analysis in *Xenopus* oocytes revealed that while the K558R variant had a significantly reduced transport activity corresponding to 47% of the wild-type activity, the remaining variants E122G, S356Y and N640I did not change the NBCe1A activity. Apparent Na^+ affinity of K558R was not different from that of wild-type NBCe1A. Immunohistological analyses in HEK293 cells and MDCK cells indicated that none of these SNPs changed the trafficking behaviors of NBCe1A. Functional analysis in HEK293 cells also revealed that only the K558R variant had a reduced transport activity, corresponding to 41% of the wild-type activity. From these results we conclude that among 4 SNPs only the K558R variant, which is predicted to lie in transmembrane segment 5, significantly reduces the NBCe1A activity without changing the trafficking behavior or the apparent extracellular Na^+ affinity.