Role of sodium pump α subunit genes for respiratory rhythm generation during perinatal period

Sodium pump (Na⁺, K⁺-ATPase) is a membrane protein that plays a critical role in maintaining Na⁺ and K⁺ gradients across the cell membrane. It consists of catalytic α and regulatory β subunits. Four α isoforms are found in mammals. In the central nervous system, the α2 isoform is mainly expressed in glial cells and α3 isoform in neuronal cells. Point mutations in the ATP1A2 (gene encoding α2 isoform in human) cause Familial hemiplegic migraine type 2 (FHM2). Point and deletion mutations in the ATP1A3 (gene encoding α3 isoform in human) cause alternating hemiplegia of childhood, apnea, and severe infantile epileptic encephalopathy often appear after birth. Through the analyses of knockout (KO) mice of the gene for α2 (Atp1a2) or for α3 (Atp1a3), here we report that both α2 and α3 subunits play important roles in respiratory rhythm generation. Homozygous Atp1a2 KO mice die shortly after birth due to respiratory malfunction resulting from abnormal Cl⁻ homeostasis in brainstem. On the other hand, homozygous Atp1a3 KO mice showed various respiratory defect. Half of Atp1a3 KO mice made an effort to breath at birth, immediately followed by seizure attack, and resulted in their death. The other showed complete absence of spontaneous body movements and no breathing movements from the very beginning at birth. Consistently, we electrophysiologically recorded various abnormal respiratory activities in the brainstem of Atp1a3 KO mice. These data suggest that both isoforms are essential for survival at perinatal period and Atp1a2 and Atp1a3 play critical, but different roles in respiratory rhythm generation.

Biography
Keiko Ikeda has completed MD, PhD from Jichi Medical University and worked as a postdoctoral fellow at Penn State University (USA) and at Genzentrum of Munchen University (Germany). Now she is a professor of Physiology in IUHW and doing experiments with her own hand.

kikeda@iuhw.ac.jp

Notes: