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学位論文名	ClC chloride channel in *Caenorhabditis elegans* （線虫クロライドチャネルの研究）
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論文内容の要旨

The ClC chloride channels are members of an expanding gene family found in bacteria, yeast, plants and animals. In mammals, at least nine ClC members have been identified,and shown to play roles in the control of muscle excitability, cell volume regulation, synaptic transmission, transepithelial transport, *etc.* The physiological relevance of chloride channels is best illustrated by three inherited human diseases (myotonia, Dent's disease and Bartter's syndrome) associated with muscle stiffness, kidney stones and renal failure caused by mutations in ClC-1 ,ClC-K 2 and ClC-5 , respectively. To have a broader basis for understanding the structures and physiological roles of chloride channels, studies with model organisms such as *Caenorhabditis elegans* or mice would be advantageous. I chose the nematode *C. elegans* as a model animal to investigate for new ClC channels.

My study focused on the structure, expression and mutant phenotypes of a putative chloride channel gene found in *C.elegans, clh-1* (ClC chloride channel homologue). The *clh-1* gene product encodes a 902 amino acid residue protein with 13 putative hydrophobic regions and is highly homologous to human ClC-1 and ClC-2 . In transgenic worms with the *lacZ* reporter gene, the *clh-1* gene was expressed predominantly in hypodermal cells including seam cells. The *clh-1* transcripts were detected in developmental stages from egg to adult. I have obtained two germ line deletion mutants [*clh-1* (*qa900*) and *clh-1* (*qa901*)] from a population of Tc 1 transposon insertional allele. Mutants were viable and behaved similarly to the wild type in terms of locomotion, pharyngeal pumping, egg laying and chemotaxis to various ions including chloride. However, they exhibited significant morphological changes characterized by an increased body width and abnormal alae structure. When mutants were cultured in hypertonic medium or introduced with a cloned *clh-1* (+) gene, they showed similar body width as the wild type. High osmolarity in the culture medium restored the normal body width of the *clh-1* mutants. This study revealed that a putative chloride channel contributes to osmotic regulation subsequently affecting the body morphology in nematodes.

論文審査の結果の要旨

本研究では、線虫 *C. elegans* の ClC クロライドチャンネル遺伝子 *clh-1* をクローニングし、その発現部位を明らかにすると共に、逆遺伝学的手法により変異体を構築した。その変異体は、培地中の浸透圧の変化に応じて身体の幅が増加する表現型を示した。この結果は、ClC クロライドチャンネルが個体レベルでの体積の調節に関与するという新たな生理学的意義を提示するものであり、博士（理学）の学位論文として十分価値があるものと認める。