CDB SEMINAR

Kouichi Iwasaki

Northwestern University Feinberg School of Medicine

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11:00~12:00 A7F CDB Conference Room

TRP channels and Magnesium homeostasis

Summary

Magnesium (Mg^{++}) is one of the most abundant cations in the human body and is involved in more than 300 enzymatic systems, including adenosine triphosphate (ATP) metabolism. Mg^{++} deficiency causes a variety of symptoms, including impaired memory, cardiac rhythm disturbances, and seizures. In spite of the biological and clinical importance of the Mg^{++} ion, little is known about the mechanism of its homeostatic regulation. It has been speculated that Mg^{++} uptake in eukaryotic cells is mainly mediated by transporters. This is partly because Mg^{++} transporters have been cloned in prokaryotic cells and partly because the antiporter that extrudes Mg^{++} in exchange for extracellular Na^{+} was identified in vertebrate cells. However, no firm evidence has been provided supporting the importance of transporters in eukaryotic Mg^{++} homeostasis.

We have investigated intestinal Mg^{++} homeostasis using the model organism C. elegans, and have discovered that the TRPM channels, GTL-1 and GON-2, play key roles in Mg^{++} homeostasis. The gon-2;gtl-1-double mutants show growth defects under low Mg^{++} conditions, and these defects can be largely rescued by dietary supplementation with excess Mg^{++}. Our electrophysiological data show that the large outwardly-rectifying current characteristic of wild type intestinal cells is mainly due to the activity of the GON-2 channel, and that GON-2 and GTL-1 play different roles in the Mg^{++} sensitivity of current generation. Two TRPM channels with different degrees of Mg^{++} responsiveness regulate appropriate intestinal electrolyte homeostasis. We propose that this type of differential regulation of intestinal electrolyte absorption ensures a constant supply of electrolytes through GTL-1, while occasional bursts of GON-2 activity allow rapid return to normal electrolyte concentrations following physiological perturbations.

Host:
Kiyoji Nishiwaki
Cell Migration, CDB
nishiwak@cdb.riken.jp
Tel:078-306-3264
(ext:1745)