No. 0909

Roles of Tight Junction in Na^+ Homeostasis and Glucose Absorption in the Small Intestine

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Summary

Many nutrients are absorbed by Na^+-coupled transport mechanism in the intestine. Yet, how the intestine meet the requirement of Na^+ for nutrient absorption remains unknown. One possible mechanism is paracellular pathway. It is contemplated that Na^+ diffuses back into the lumen via its pathway because of the lumen-negative potential difference induced by Na^+-coupled transport. The claudin family of transmembrane tight junction proteins is critical in determining the paracellular ionic permeability and selectivity. To investigate the role of paracellular Na^+ permeability for Na^+-coupled glucose absorption, we used claudin-15 knockout (cldn15$^{-/-}$) mice and measured the electric parameters in Ussing chambers. Moreover, we determined the absorption rate of glucose and Na^+ by intestinal perfusion *in vivo*. The electric conductance in cldn15$^{-/-}$ mice was decreased compared to that in the wild mice (18 vs. 41 mS/cm^2). Dilution potential (DP) was measured while lowering apical NaCl concentration. DP was significantly decreased in cldn15$^{-/-}$ mice compared to that in wild mice (-0.5 vs 9.7 mV). From this results permeability ratio (P_{Na}/P_{Cl}) between Na^+ and Cl^- for paracellular pathways was estimated to be decreased in cldn15$^{-/-}$ mice (1.0 vs. 3.2). When the jejunum was perfused with 15 mM Na^+ solution without glucose, Na^+ absorption was observed in cldn15$^{-/-}$ mice while Na^+ secretion in wild mice. Addition of glucose to the pefusate caused an increase of Na^+ absorption in cldn15$^{-/-}$ mice but not in wild mice. These results suggest that Na^+ is rapidly recycled from blood side to the lumen presumably through the cldn15-based, cation selective paracellular pore to maintain the Na^+-dependent glucose absorption.