Molecular function analysis on the role of TRPV6 in the onset of digestive system disease

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In biological systems, the calcium ion (Ca^{2+}) play an important role as a second messenger. Failure to regulate Ca^{2+} signaling can cause various diseases. It has been reported that the defect of Ca^{2+} signaling is related to the onset of a certain digestive system disease, and mutations of Transient Receptor Potential cation channel subfamily V member 6 (TRPV6) was identified from genetic screening of a patient. TRPV6 is a member of the TRP channel family which regulates Ca^{2+} influx from outside the cell, and is a Ca^{2+} channel that is expressed in various tissues such as small intestine, kidney, pancreas, and prostate. TRPV6 exhibits high Ca^{2+} selectivity and transports Ca^{2+} into the cell according to the concentration gradient, functioning as the initial step of Ca^{2+} transport pathway. In this study, we focused on the possibility that the genetic mutations of TRPV6 obtained from a genetic screening of a large number of patients of different races are involved in the development of the digestive system disease and analyzed the function of TRPV6 mutants using Ca^{2+} imaging, Western blotting (WB), and electrophysiology. In Ca^{2+} imaging analysis, many mutants demonstrated functional changes. WB revealed the changes of expression pattern in certain mutants. There was a clear correlation between the results of Ca^{2+} imaging and WB. Moreover, in the electrophysiological analysis, some mutants exhibited current characteristics different from wild type. These results suggest that functional changes due to mutations in TRPV6 are involved in disease development.