Abstract

The transient receptor potential ankyrin 1 (TRPA1) ion channel is expressed in a subset of primary afferent neurones where it is activated by a variety of pungent and chemically reactive compounds such as allyl isothiocyanate or cinnamaldehyde. This voltage-dependent channel is activated through covalent modification of cytoplasmic cysteines and, from the cytoplasmic side, is also critically regulated by calcium ions. Both, amino (N-) and carboxyl (C-) termini have been shown to be involved in these processes. Using electrophysiological and molecular-biology techniques, we explored the role of specific cytoplasmic domains in the activation of TRPA1. By measuring chemically-, voltage-, and calcium-activated membrane TRPA1-mediated currents, we identified highly conserved serine and threonine residues along the N-terminal ankyrin repeat domain, mutation of which strongly affected responses of the channel. In addition, using C-terminally truncated construct previously reported to be involved in calcium regulation, we present a new finding that the distal C-terminal tail contributes to voltage-dependent activation of TRPA1.