Acid-sensing ion channel 1a is involved in long-term depression in the rodent hippocampus

D. Mango[1], G. Battaglia[2], M. Feligioni[1], Z.I. Bashir[3], F. Nicoletti[2], R. Nisticò[1,4]

[1]European Center for Brain Research, Rome, Italy
[2]Dept. of Molecular Pathology, I.R.C.C.S. Neuromed, Pozzilli, Italy
[3]Dept. of Physiology and Pharmacology, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, United Kingdom
[4]Dept. of Biology, University of Rome Tor Vergata, Rome, Italy

Acid-sensing ion channels (ASICs), members of the degenerin/epithelial Na^+ channel superfamily, are widely distributed in the mammalian nervous system. ASIC1a are highly permeable to Ca^{2+} and are localized in different brain regions with high synaptic density. ASIC1a activation has crucial importance in numerous physiological and pathological processes, including synaptic plasticity, learning and memory. In these processes, a prominent hypothesis is that activation of postsynaptic ASIC1a promotes depolarization, thereby interacting with *N*-methyl-D-aspartate receptor function thus contributing to the induction of synaptic plasticity.

To shed some light on the involvement of ASIC1a in synaptic plasticity, we studied long-term depression (LTD) in hippocampus by employing pharmacological and genetic approaches. Using whole-cell patch clamp recordings on hippocampal slices, we found that the selective ASIC1a blocker Psalmotoxin-1 inhibits current-evoked firing discharge of CA1 pyramidal neurons. Next, we show that Psalmotoxin-1 and amiloride are able to reduce the magnitude of CA1-LTD without any effect on excitatory synaptic transmission. Our results highlight a novel role for ASIC1a channels in different forms of LTD in young and adult mice. These findings support a crucial modulatory role of ASIC1a channels in hippocampal LTD, suggesting that this class of proteins might represent a novel therapeutic target for the treatment of neuroplasticity disorders.