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# Acid-sensing (proton-gated) ion channels (ASICs) (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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## Abstract

Acid-sensing ion channels (ASICs, **nomenclature as agreed by NC-IUPHAR [35]**) are members of a $Na^+$ channel superfamily that includes the epithelial $Na^+$ channel (ENaC), the FMRF-amide activated channel (FaNaC) of invertebrates, the degenerins (DEG) of *Caenorhabitis elegans*, channels in *Drosophila melanogaster* and 'orphan' channels that include BLINaC [46] and INaC [47] that have also been named BASICs, for bile acid-activated ion channels [58]. ASIC subunits contain two TM domains and assemble as homo- or hetero-trimers [34, 31, 5] to form proton-gated, voltage-insensitive, $Na^+$ permeable, channels (reviewed in [33, 57]). Splice variants of ASIC1 [termed ASIC1a (ASIC, ASICα, BNaC2α) [55], ASIC1b (ASICβ, BNaC2β) [13] and ASIC1b2 (ASICβ2) [50]; note that ASIC1a is also permeable to $Ca^{2+}$] and ASIC2 [termed ASIC2a (MDEG1, BNaC1α, BNC1α) [45, 56, 30] and ASIC2b (MDEG2, BNaC1β) [40]] have been cloned. Unlike ASIC2a (listed in table), heterologous expression of ASIC2b alone does not support $H^+$-gated currents. A third member, ASIC3 (DRASIC, TNaC1) [54], has been identified. A fourth mammalian member of the family (ASIC4/SPASIC) does not support a proton-gated channel in heterologous expression systems and is reported to downregulate the expression of ASIC1a and ASIC3 [1, 32, 24, 39]. ASIC channels are primarily expressed in central and peripheral neurons including nociceptors where they participate in neuronal sensitivity to acidosis. They have also been detected in taste receptor cells (ASIC1-3), photoreceptors and retinal cells (ASIC1-3), cochlear hair cells (ASIC1b), testis (hASIC3), pituitary gland (ASIC4), lung epithelial cells (ASIC1a and -3), urothelial cells, adipose cells (ASIC3), vascular smooth muscle cells (ASIC1-3), immune cells (ASIC1,-3 and -4) and bone (ASIC1-3). A neurotransmitter-like function of protons has been suggested, involving postsynaptically located ASICs of the CNS in functions such as learning and fear perception [25, 36, 63], responses to focal ischemia [59] and to axonal degeneration in autoimmune inflammation in a mouse model of multiple sclerosis [29], as well as seizures [64] and pain [19, 20, 10, 22]. Heterologously expressed heteromultimers form ion channels with differences in kinetics, ion selectivity, pH- sensitivity and sensitivity to blockers that resemble some of the native proton activated currents recorded from neurones [40, 3, 28, 8].



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ASIC2
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=685

ASIC3
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=686

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