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Aquaporins (version 2020.4) in the IUPHAR/BPS Guide to Pharmacology Database

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Abstract

Aquaporins and aquaglyceroporins are membrane channels that allow the permeation of water and certain other small solutes across the cell membrane, or in the case of AQP6, AQP11 and AQP12A, intracellular membranes, such as vesicles and the endoplasmic reticulum membrane [17]. Since the isolation and cloning of the first aquaporin (AQP1) [21], 12 additional mammalian members of the family have been identified, although little is known about the functional properties of one of these (*AQP12A*; Q8IXF9) and it is thus not tabulated. The other 12 aquaporins can be broadly divided into three families: orthodox aquaporins (AQP0,-1,-2,-4,-5, -6 and -8) permeable mainly to water, but for some additional solutes [5]; aquaglyceroporins (AQP3,-7 -9 and -10), additionally permeable to glycerol and for some isoforms urea [16], and superaquaporins (AQP11 and 12) located within cells [14]. Some aquaporins also conduct ammonia and/or H_2O_2 giving rise to the terms 'ammoniaporins' ('aquaammoniaporins') and 'peroxiporins', respectively. Aquaporins are impermeable to protons and other inorganic and organic cations, with the possible exception of AQP1 [16]. One or more members of this family of proteins have been found to be expressed in almost all tissues of the body [reviewed in Yang (2017) [27]]. AQPs are involved in numerous processes that include systemic water homeostasis, adipocyte metabolism, brain oedema, cell migration and fluid secretion by epithelia and loss of function mutations of some human AQPs, or their disruption by autoantibodies further underscore their importance [reviewed by Verkman *et al*. (2014) [24], Kitchen *et al.* (2105) [16]].

Functional AQPs exist as homotetramers that are the water conducting units wherein individual AQP subunits (each a protomer) have six transmembrane helices and two half helices that constitute a seventh 'pseudotransmembrane domain' that surrounds a narrow water conducting channel [17]. In addition to the four pores contributed by the protomers, an additional hydrophobic pore exists within the center of the complex [17] that may mediate the transport of gases (*e.g.* O_2, CO_2, NO) and cations (the central pore is the proposed transport pathway for cations through AQP1) by some AQPs [8, 15]. Although numerous small molecule inhibitors of aquaporins, particularly APQ1, have been reported primarily from *Xenopus* oocyte swelling assays, the activity of most has subsequently been disputed upon retesting using assays of water transport that are less prone to various artifacts [6] and they are therefore excluded from the tables [see Tradtrantip*et al.* (2017) [23] for a review].

Contents

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Database links

Aquaporins
http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=119
Channels and Subunits
AQP0
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=687
AQP1
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=688
AQP2
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=689
AQP3
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=690
AQP4
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=691
AQP5
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=692
AQP6
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=693
AQP7
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=694
AQP8
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=695
AQP9
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=696
AQP10
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=697
AQP11
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3062

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