

Aquaporins (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

Alex C. Conner¹

1. University of Birmingham, UK

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 [9]. Since the isolation and cloning of the first aquaporin (AQP1) [10], 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 [2]; aquaglyceroporins (AQP3,-7 -9 and -10), additionally permeable to glycerol and for some isoforms urea [8], and superaquaporins (AQP11 and 12) located within cells [5]. Some aquaporins also conduct ammonia and/or H₂O₂ 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 [8]. 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) [13]]. 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) [12], Kitchen *et al.* (2105) [8]].

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 [9]. In addition to the four pores contributed by the protomers, an additional hydrophobic pore exists within the center of the complex [9] that may mediate the transport of gases (*e.g.* O₂, CO₂, NO) and cations (the central pore is the proposed transport pathway for cations through AQP1) by some AQPs [4, 6]. 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 [3] and they are therefore excluded from the tables [see Tradtrantipet *et al.* (2017) [11] for a review].

Contents

This is a citation summary for Aquaporins in the [Guide to Pharmacology](#) database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here

under database links.

[GtoPdb](#) is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts.

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

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>

References

1. Castle NA. (2005) Aquaporins as targets for drug discovery. *Drug Discov. Today* **10**: 485-93
[\[PMID:15809194\]](#)
2. Day RE, Kitchen P, Owen DS, Bland C, Marshall L, Conner AC, Bill RM and Conner MT. (2014) Human aquaporins: regulators of transcellular water flow. *Biochim. Biophys. Acta* **1840**: 1492-506
[\[PMID:24090884\]](#)
3. Esteva-Font C, Jin BJ, Lee S, Phuan PW, Anderson MO and Verkman AS. (2016) Experimental Evaluation of Proposed Small-Molecule Inhibitors of Water Channel Aquaporin-1. *Mol. Pharmacol.* **89**: 686-

93 [PMID:26993802]

4. Geyer RR, Musa-Aziz R, Qin X and Boron WF. (2013) Relative CO₂/NH₃ selectivities of mammalian aquaporins 0-9. *Am. J. Physiol., Cell Physiol.* **304**: C985-94 [PMID:23485707]
5. Ishibashi K, Tanaka Y and Morishita Y. (2014) The role of mammalian supraaquaporins inside the cell. *Biochim. Biophys. Acta* **1840**: 1507-12 [PMID:24189537]
6. Kaldenhoff R, Kai L and Uehlein N. (2014) Aquaporins and membrane diffusion of CO₂ in living organisms. *Biochim. Biophys. Acta* **1840**: 1592-5 [PMID:24141139]
7. King LS, Kozono D and Agre P. (2004) From structure to disease: the evolving tale of aquaporin biology. *Nat. Rev. Mol. Cell Biol.* **5**: 687-98 [PMID:15340377]
8. Kitchen P, Day RE, Salman MM, Conner MT, Bill RM and Conner AC. (2015) Beyond water homeostasis: Diverse functional roles of mammalian aquaporins. *Biochim. Biophys. Acta* **1850**: 2410-21 [PMID:26365508]
9. Kreida S and Törnroth-Horsefield S. (2015) Structural insights into aquaporin selectivity and regulation. *Curr. Opin. Struct. Biol.* **33**: 126-34 [PMID:26342685]
10. Preston GM, Carroll TP, Guggino WB and Agre P. (1992) Appearance of water channels in *Xenopus* oocytes expressing red cell CHIP28 protein. *Science* **256**: 385-7 [PMID:1373524]
11. Tradtrantip L, Jin BJ, Yao X, Anderson MO and Verkman AS. (2017) Aquaporin-Targeted Therapeutics: State-of-the-Field. *Adv. Exp. Med. Biol.* **969**: 239-250 [PMID:28258578]
12. Verkman AS, Anderson MO and Papadopoulos MC. (2014) Aquaporins: important but elusive drug targets. *Nat Rev Drug Discov* **13**: 259-77 [PMID:24625825]
13. Yang B. (2017) Aquaporins *In Advances in Experimental Medicine and Biology* Edited by Yang B: Springer: 1-276 [ISBN: 9789402410570]
14. Yasui M, Hazama A, Kwon TH, Nielsen S, Guggino WB and Agre P. (1999) Rapid gating and anion permeability of an intracellular aquaporin. *Nature* **402**: 184-7 [PMID:10647010]