P-type ATPases (EC 3.6.3.-)

Phosphorylation-type ATPases are associated with membranes and the transport of ions or phospholipids. A characteristic is the interconversion between E1 and E2 conformations in the activity cycle of the transporters.

Na^+/K^+-ATPase (EC 3.6.3.9)

The cell-surface Na^+/K^+-ATPase is an integral membrane protein that regulates the membrane potential of the cell by maintaining gradients of Na^+ and K^+ ions across the plasma membrane, also making a small, direct contribution to membrane potential, particularly in cardiac cells. The active enzyme is a heteromultimer with incompletely defined stoichiometry, possibly as tetramers of heterodimers, each consisting of one of four large, 10TM catalytic α subunits and one of three smaller 1TM glycoprotein β-subunits (see table). Additional protein partners known as FXYD proteins (e.g. FXYD2, ENSG00000137731) appear to associate with and regulate the activity of the pump.

Nomenclature	Systematic name	Ensembl ID	Other names
α1	ATP1A1	ENSG00000163399	Sodium/potassium-transporting ATPase subunit α-1, sodium pump subunit α-1, Na^+/K^+ ATPase α-1 subunit
α2	ATP1A2	ENSG00000018625	Sodium/potassium-transporting ATPase subunit α-1, sodium pump subunit α-1, Na^+/K^+ ATPase α-1 subunit
α3	ATP1A3	ENSG00000105409	Sodium/potassium-transporting ATPase subunit α-3, sodium pump subunit α-3, Na^+/K^+ ATPase α-3 subunit
α4	ATP1A4	ENSG00000132681	Sodium/potassium-transporting ATPase subunit α-4, sodium pump subunit α-4, Na^+/K^+ ATPase α-4 subunit
β1	ATP1B1	ENSG00000143153	Sodium/potassium-transporting ATPase subunit β-1
β2	ATP1B2	ENSG00000129244	Sodium/potassium-transporting ATPase subunit β-2
β3	ATP1B3	ENSG00000069849	Sodium/potassium-transporting ATPase subunit β-3, CD298 antigen

Inhibited by ouabain and cardiac glycosides, such as digoxin, as well as potentially endogenous cardiotonic steroids (see Bagrov *et al*., 2009).

Ca^{2+}-ATPases (EC 3.6.3.8)

The sarcoplasmic/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) is an intracellular membrane-associated pump for sequestering calcium from the cytosol into intracellular organelles, usually associated with the recovery phase following excitation of muscle and nerves.

Nomenclature	Systematic name	Ensembl ID	Other names
SERCA1	ATP2A1	ENSG00000196296	Sarcoplasmic/endoplasmic reticulum calcium ATPase 1, fast twitch skeletal muscle isoform
SERCA2	ATP2A2	ENSG00000174437	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2, calcium pump 2, slow twitch skeletal muscle isoform
SERCA3	ATP2A3	ENSG00000074370	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3

The fungal toxin ochratoxin A has been described to activate SERCA in kidney microsomes (Chong & Rahimtula, 1992). Cyclopiazonic acid (Seidler *et al*., 1989) and thapsigargin (Lytton *et al*., 1991) are widely employed to block SERCA. Thapsigargin has also been described to block the TRPV1 vanilloid receptor (Toth *et al*., 2002).

The plasma membrane Ca^{2+}-ATPase (PMCA) is a cell-surface pump for extruding calcium from the cytosol, usually associated with the recovery phase following excitation of cells. The active pump is a homodimer, each subunit of which is made up of ten transmembrane segments, with cytosolic C- and N-termini and two large intracellular loops.

Nomenclature	Systematic name	Ensembl ID	Other names
PMCA1	ATP2B1	ENSG00000070961	Plasma membrane calcium ATPase isoform 1
PMCA2	ATP2B2	ENSG00000157087	Plasma membrane calcium ATPase isoform 2
PMCA3	ATP2B3	ENSG00000067842	Plasma membrane calcium ATPase isoform 3
PMCA4	ATP2B4	ENSG00000058668	Plasma membrane calcium ATPase isoform 4, matrix-remodelling-associated protein 1

The stoichiometry of flux through the PMCA differs from SERCA, with the PMCA transporting 1 Ca^{2+} while SERCA transports 2 Ca^{2+}.

Secretory pathway Ca^{2+}-ATPases (SPCA) allow accumulation of calcium and manganese in the Golgi apparatus.

Nomenclature	Systematic name	Ensembl ID	Other names
SPCA1	ATP2C1	ENSG00000017260	ATPase 2C1, ATP-dependent Ca^{2+} pump PMR1
SPCA2	ATP2C2	ENSG00000064270	ATPase 2C2, secretory pathway Ca^{2+}-ATPase 2

Loss-of-function mutations in SPCA1 appear to underlie Hailey–Hailey disease (Hu *et al.*, 2000).

H^+/K^+-ATPase (EC 3.6.3.10)

The H^+/K^+ ATPase is a heterodimeric protein, made up of α and β subunits. The α subunit has 10 transmembrane domains and exhibits catalytic and pore functions, while the β subunit has a single transmembrane domain, which appears to be required for intracellular trafficking and stabilising the α subunit. The ATP4A and ATP4B subunits are expressed together, while the ATP12A subunit is suggested to be expressed with the β1 (ATP1B1) subunit of the Na^+/K^+-ATPase (Pestov *et al.*, 2006).

Nomenclature	Ensembl ID	Other names
ATP4A	ENSG00000105675	Potassium-transporting ATPase α chain 1, gastric H^+/K^+-ATPase α subunit, ATP6A
ATP12A	ENSG00000075673	Potassium-transporting ATPase α chain 2, non-gastric H^+/K^+-ATPase α subunit, ATP1AL1
ATP4B	ENSG00000186009	Potassium-transporting ATPase β chain 1, gastric H^+/K^+-ATPase β subunit

The gastric H^+/K^+-ATPase is inhibited by (*R*)-lansoprazole and a metabolite of (*S*)-omeprazole.

Cu^{2+}-ATPase (EC 3.6.3.4)

Copper-transporting ATPases convey copper ions across cell-surface and intracellular membranes. They consist of eight transmembrane domains and associate with multiple copper chaperone proteins (e.g. ATOX1, ENSG00000177556).

Nomenclature	Ensembl ID	Other names
ATP7A	ENSG00000165240	Copper-transporting ATPase 1, copper pump 1, Menkes disease-associated protein
ATP7B	ENSG00000123191	Copper-transporting ATPase 2, copper pump 2, Wilson disease-associated protein

Phospholipid-transporting ATPase (EC 3.6.3.1)

These transporters are thought to translocate the aminophospholipids phosphatidylserine and phosphatidylethanolamine from one side of the phospholipid bilayer to the other.

Nomenclature	Ensembl ID	Other names
ATP8A1	ENSG00000124406	Probable phospholipid-transporting ATPase IA, chromaffin granule ATPase II
ATP8A2	ENSG00000132932	Probable phospholipid-transporting ATPase IB, ML-1
ATP8B1	ENSG00000081923	Probable phospholipid-transporting ATPase IC, familial intrahepatic cholestasis type 1
ATP8B2	ENSG00000143515	Probable phospholipid-transporting ATPase ID
ATP8B3	ENSG00000130270	Probable phospholipid-transporting ATPase IK
ATP8B4	ENSG00000104043	Probable phospholipid-transporting ATPase IM
ATP9A	ENSG00000054793	Probable phospholipid-transporting ATPase IIA, ATPase IIA
ATP9B	ENSG00000166377	Probable phospholipid-transporting ATPase IIB, ATPase class II type 9B
ATP10A	ENSG00000206190	Probable phospholipid-transporting ATPase VA, ATPase class V type 10A, aminophospholipid translocase VA, ATP10C
ATP10B	ENSG00000118322	Probable phospholipid-transporting ATPase VB, ATPase class V type 10B
ATP10D	ENSG00000145246	Probable phospholipid-transporting ATPase VD, ATPase class V type 10D
ATP11A	ENSG00000068650	Probable phospholipid-transporting ATPase IH, ATPase class VI type 11A, ATPase IS
ATP11B	ENSG00000058063	Probable phospholipid-transporting ATPase IF, ATPase class VI type 11B, ATPase IR
ATP11C	ENSG00000101974	Probable phospholipid-transporting ATPase IG, ATPase class VI type 11C, ATPase IG, ATPase IQ

Loss-of-function mutations in ATP8B1 are associated with type I familial intrahepatic cholestasis.

A further series of structurally-related proteins have been identified in the human genome, with as yet undefined function, including ATP13A1 (ENSG00000105726), ATP13A2 (ENSG00000159363), ATP13A3 (ENSG00000133657), ATP13A4 (ENSG00000127249) and ATP13A5 (ENSG00000187527).

Further Reading

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