P2RX7 (purinergic receptor P2X, ligand-gated ion channel, 7)

Pablo Pelegrin, Annmarie Surprenant

Faculty of Life Science, Michael Smith Building, University of Manchester, Manchester, M13 9PT, UK

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Identity
Hugo: P2RX7
Other names: MGC20089; P2X7; P2Z
Location: 12q24.31

DNA/RNA
Description
The P2RX7 gene is comprised of 13 coding exons.

Transcription
The full length transcript is 3135 bp long and 10 alternative splicing isoforms have been identified.

Pseudogene
Not known.

Protein
Description
The protein has 595 residues amino acids and compromises a 69 kDa calculated molecular weight. However, N-glycosylation in the extracellular loop increases the size of the P2X7 receptor to about 75-85 kDa; the protein is composed successively (from the N-to the C-terminus) by:
- 25 amino acid intracellular N-terminus
- 21 amino acid first transmembrane domain
- 288 amino acid extracellular loop
- 21 amino acid second transmembrane domain
- 240 amino acid intracellular C-terminal region

Expression
In a wide variety of tissues including heart, liver, pancreas, thymus, skeletal muscle and brain, although in brain the expression is mainly restricted to microglia. It also has relevant expression and function in immune cells (mainly in antigen presenting cells, such as monocytes, macrophages and dendritic cells).

Localisation
Mainly is found in the plasma membrane, however it also can be found in intracellular membrane compartments while trafficking to the plasma membrane.

Function
Acts as a ligand gated ion channel, sensing high concentration of extracellular ATP. Responsible for ATP-dependent activation and release of proinflammatory cytokines of the interleukin-1 family, mainly interleukin-1beta, interleukin-18 and interleukin-1alpha, playing a pivotal role in inflammatory responses. Prolonged stimulation of the P2X7 receptor can lead to plasma membrane bleb formation, opening of pannexin-1 dependent membrane pores and eventual cell death.

Homology
With other P2X receptors, with the higher homology with P2RX4. Excluding the unique C-terminal domain, homology is 39-49% with other P2X receptors.

Mutations
Germinal
The human P2X7 receptor gene is highly polymorphic and more then 260 SNP have been described, only four loss-of-function and one gain-of-function SNP have been described to date:
- Loss of protein function:
  946 G to A (Arg-307 to Gln)
  1068 G to A (Ala-348 to Thr)
  1513 A to C (Glu-496 to Ala)
  1729 T to A (Ile-568 to Asp)
- Gain of protein function: 489 C to T (His-155 to Tyr)

Somatic
Not known in human.

Implicated in

Extrapulmonary tuberculosis

Note: The P2RX7 1513C allele has been strongly associated with extrapulmonary tuberculosis. The allele was associated with a reduced killing of Mycobacterium tuberculosis by macrophages.

Chronic lymphoid leukemia (CLL)

Note: The 1513C allele of P2RX7 has been associated with the clinical course of patients affected by chronic lymphocytic leukemia (CLL). There is a possible role for the P2X7 receptor in the susceptibility to familial CLL or, alternately, the 1513C allele may be in linkage disequilibrium with a nearby susceptibility gene.

Various cancers, including breast cancer, prostate cancer, papillary thyroid cancer and neuroblastoma

Note: P2X7 receptor is overexpressed in a variety of cancers (see above). A detailed understanding of the mechanistic contribution mediated by P2RX7 has yet to be established. However, there is substantial evidence that the P2X7 receptor may mediate cell survival and growth by increasing the efficiency of oxidative phosphorylation and total intracellular ATP stores. Finally it has been proposed that the P2X7 receptor may be a candidate marker of papillary thyroid cancer.

References


Pelegrin P, Surprenant A. Pannexin-1 mediates large pore formation and interleukin-1beta release by the ATP-gated P2X7 receptor. EMBO J 2006;25:5071-5082.


This article should be referenced as such: