P2X7R

The P2X receptor 7 (P2X7R) is a plasma membrane receptor sensing extracellular ATP associated with a wide variety of cellular functions. It is most commonly expressed on immune cells and is highly upregulated in a number of human cancers where it can play a trophic role in tumorigenesis.

P2X purinoceptor 7 is a protein that in humans is encoded by the P2RX7 gene.

The product of this gene belongs to the family of purinoceptors for ATP. Multiple alternatively spliced variants which would encode different isoforms have been identified although some fit nonsense-mediated decay criteria.

The receptor is found in the central and peripheral nervous systems, in microglia, in macrophages, in the uterine endometrium, and in the retina.

The P2X7 receptor also serves as a pattern recognition receptor for extracellular ATP-mediated apoptotic cell death, regulation of receptor trafficking, mast cell degranulation, and inflammation.

Activation of this receptor leads to the formation of a non-selective cation channel, which has been associated with several cellular functions mediated by the PI3K/Akt pathway and protein kinases. Due to its broad range of functions, the receptor represents a potential therapeutic target for a number of cancers.

A review describes the range of mechanisms associated with P2X7R activation in cancer settings and highlights the potential of targeted inhibition of P2X7R as a therapy. It also describes in detail a number of key P2X7R antagonists currently in pre-clinical and clinical development, including oxidized ATP, Brilliant Blue G (BBG), KN-62, KN-04, A740003, A438079, GSK1482160, CE-224535, JNJ-54175446, JNJ-55308942, and AZ10606120. Lastly, it summarises the in vivo studies and clinical trials associated with the use and development of these P2X7R antagonists in different disease contexts [1)].

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Drill M, Jones NC, Hunn M, O'Brien TJ, Monif M. Antagonism of the ATP-gated P2X7 receptor: a potential therapeutic strategy for cancer. Purinergic Signal. 2021 Mar 17. doi: 10.1007/s11302-021-09776-9. Epub ahead of print. PMID: 33728582.