EXTRACELLULAR MG^{2+} MODULATES C-TERMINAL TAIL DEPENDENT P2X7 RECEPTOR FUNCTIONAL PROPERTIES

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The cytolytic P2X7 purinoceptor (P2X7R: 595 amino acids in length) is an ATP-gated cation channel that can convert to a non-selective pore. The cytosolic C-terminal tail of the P2X7R is thought to modulate this function. The present study aimed to characterise functional role of this C-terminal tail in P2X7 agonist 3'-O-(4-benzoyl)benzoyl adenosine 5'-triphosphate (BzATP) activated current by applying the whole-cell configuration of the patch-clamp technique and intracellular calcium ($[Ca^{2+}]_i$) increase by microfluorimetric experiments.
In HEK-293 cells expressing P2X7R, BzATP-evoked currents, in physiological extracellular solution, were concentration-dependent. Upon repeated stimulations at low agonist concentrations the channel expands to accommodate large molecules such as N-methyl-D-glucamine ($NMDG^+$). Removal of extracellular Mg^{2+} increased the inward Na^+ and $NMDG^+$ currents about 2-fold, causing a shift in the dose-response curves.
By contrast, in HEK-293 cells expressing truncated P2X7 receptor at residue 375 (of 595), that lacks the entire intracellular carboxy terminus, the amplitude of Na^+ currents activated by high concentrations of BzATP were very small and $NMDG^+$ current was absent in the presence of physiological as well as low Mg^{2+} concentrations.
On the contrary, in these cells the absence of Mg^{2+} increased BzATP-activated calcium influx and the $[Ca^{2+}]_i$ signal was comparable to wild-type P2X7R.
These findings confirm that C-terminal tail of P2X7R has an important role in the permeability of the pore dramatically reducing the Na^+ influx and losing the extracellular Mg^{2+} control. By contrast, the $[Ca^{2+}]_i$ level is partially affected by truncation and extracellular Mg^{2+} is efficient on $[Ca^{2+}]_i$ signal. We suggest that cytoplasmic tail deleted variant, highly expressed in various tissues, could have physiological roles without functions of the downstream apoptotic induction and pore formation.