Unveil the role of Adenosine A2a receptor variation in IP3 level through cAMP dependent PKA for the modulation of [Ca^{2+}]i

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A2A receptors coupled to Gs/olf protein and activate Adenylyl cyclase (AC) leading to the release of cAMP, activation of cAMP-dependent PKA, phosphorylation of cAMP responsive element binding protein, ERK. In this study, we investigate the possible role of A2AR in modulation of free cytosolic Ca2+ concentration ([Ca2+] i) via cAMP and PKA signalling in stably transfected HEK293 cells. HEK293 cells were induced by A2A receptor agonist 5'-N-ethylcarboxamide adenosine (NECA) and A2A receptor antagonist, ZM-241385 and caffeine. The Ca 2+, IP3 and cAMP levels were measured by Fluo-4AM and Enzyme immunoassay detection method respectively. Moreover, cAMP dependent PKA were determined using PepTag® Non-Radioactive Detection. The Ca 2+ level was elevated with NECA while decrease with ZM241385 and caffeine. Surprisingly, with pre-treatment of PTX (perussis toxin) the release of IP3 (Inositol 1,4,5-trisphosphate) was observed which stimulates Ca 2+ release from the Endoplasmic sreticulum while decreases with ZM241385 and caffeine. The further evidences also suggests that downstream signaling like cAMP and PKA was elevated in the presence of A2A agonist NECA. Essentially, reverse effect was observed with A2A antagonist ZM241385 and caffeine. However, pre-treatment of PTX and selective cAMP dependent PKA inhibitor, the level of IP3 remained unaffected by either A2A receptors agonist or antagonist. Hence, the study demonstrated that Adenosine A2A receptor has IP3 - evoked Ca 2+ signaling where the response is potentiated via cAMP/ cAMP dependent PKA.

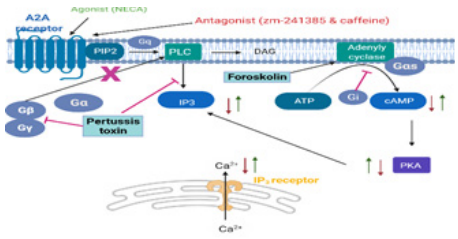

Fig: Schematic representation of the calcium signaling pathways via A2aR in stably transfected A2aR cDNA in HEK293 cells. Based on the results of the present study, we observed that A2aR coupled to Gαs /AC/cAMP/PKA signalling in HEK293 cells where PKA phosphorylation results in the modulating of IP3 level. Therefore, calcium signalling via A2aR is IP3 dependent. Upward Arrow line indicate increase/ activation and downward arrow line indicate decrease/inactivation. Blunt end line represents inhibition. Figure was generated using biorender

Speaker Biography

Tuithung Sophronea is currently a Ph.D. Researcher at Dr. B.R Ambedkar Center for Biomedical Research, University of Delhi, India. She has done her B.Tech in Biotechnology from Sardar Vallabh Bhai Patel University of Agriculture and Technology, her MSc Biotechnology in Indian Institute of Technology, Bombay, and her Ph.D. from Delhi University in the field of Biomedical/Medical Engineering.

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