$P2Y_1$ and $P2Y_2$ receptor distribution varies along the human placental vascular tree: role of nucleotides in vascular tone regulation

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Abstract

The expression of purinergic P2Y receptors (P2YRs) along the cord, superficial chorionic vessels and cotyledons of the human placenta was analysed and functional assays were performed to determine their vasomotor activity. Immunoblots for the $P2Y_1R$ and $P2Y_2R$ revealed a 6- to 8-fold increase in receptor expression from the cord to the chorionic or cotyledon vessels. In the cord and chorionic vessels the receptor distribution was mainly in the smooth muscle, whereas in the cotyledon vessels these receptors were equally distributed between the endothelium and smooth muscle cells. An exception was the $P2Y_2R$ at the umbilical artery, which was distributed as in the cotyledon. mRNA coding for the $P2Y_1R$ and $P2Y_2R$ were detected by RT-PCR and the mRNA coding for the $P2Y_4R$, $P2Y_6R$ and $P2Y_{11}R$ was also identified. Application of 2-MeSADP and uridine triphosphate (UTP), preferential $P2Y_1R$ and $P2Y_2R$ ligands, respectively, resulted in contraction of isolated rings from umbilical and chorionic vessels. The vasoconstriction was blocked in a concentration-dependent manner by 10–100 nM indomethacin or 10 nM GR32191, suggesting the involvement of thromboxane receptors. MRS 2179, a selective $P2Y_1R$ antagonist, reduced the 2-MeSADP- but not the UTP-evoked contractions. Perfusion of cotyledons with 2-MeSADP or UTP evoked concentration-dependent reductions in perfusion pressure mediated by the NO–cGMP pathway. Blockade of NO synthase abolished the vasodilatation and the rise in luminal NO elicited by either agonist. MRS 2179 antagonized the dilatation and rise in luminal NO evoked by 2-MeSADP but not by UTP. In summary, $P2Y_1R$ and $P2Y_2R$ are unevenly distributed along the human placental vascular tree; both receptors are coupled to different signalling pathways in the cord/chorionic vessels *versus* the cotyledon leading to opposing vasomotor responses.