Inhibition of ecto-ATPase by PPADS, suramin and reactive blue in endothelial cells, C6 glioma cells and RAW 264.7 macrophages

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摘要

Abstract

1. Previous studies have shown that bovine pulmonary artery endothelium (CPAE) has P2Y and P2U purinoceptors, rat C6 glioma cells have P2U purinoceptors and mouse RAW 264.7 cells have pyrimidinoceptors, all of which are coupled to phosphoinositide-specific phospholipase C (PI-PLC). The dual actions of PPADS, suramin and reactive blue as antagonists of receptor subtypes and ecto-ATPase inhibitors were studied in these three cell types. 2. In CPAE, suramin, at 3-100 microM, competitively inhibited the PI responses induced by 2MeSATP and UTP, with pA2 values of 5.5 +/- 0.3 and 4.4 +/- 0.4, respectively. Reactive blue, at 1-3 microM, produced shifts to the right of the 2MeSATP and UTP curves, but no further right shift at 10 microM. PPADS, at 10 microM, caused a 3 fold right shift of the 2MeSATP curve, but no further shift at concentrations up to 100 microM. In contrast, a dose-dependent shift to the left of the UTP curve and a weak inhibition of the ATP response were seen with PPADS. 3. In RAW 264.7 cells, suramin and reactive blue, but not PPADS, competitively inhibited the UTP response, with pA2 values of 4.8 +/- 0.5 and 5.8 +/- 0.7, respectively. 4. In C6 glioma cells, although suramin and reactive blue inhibited the ATP response, a potentiation effect on ATP and UTP responses was seen with PPADS. 5. The ecto-ATPase inhibitory activity of these three receptor antagonists were determined. All three inhibited ecto-ATPase present in CPAE, C6 and RAW 264.7 cells, with IC50 values of 4, 4.8 and 4.7 for PPADS, 4, 4.4 and > > 4 for suramin, and 4.5, 4.7 and 4.7 for reactive blue. 6. This study indicates that PPADS, suramin and reactive blue ar ecto-ATPase inhibitors. This property, combined with their antagonistic selectivity for receptor subtypes, can result in inhibition of, potentiation of, or lack of effect on agonist-mediated PI responses. Reactive blue is a

more potent antagonist than suramin on P2Y, P2U and pyrimidinoceptors, and PPADS is a weak antagonist for P2Y receptors.