Purinoceptors in renal microvessels: adenosine-activated and cytochrome P450 monooxygenase-derived arachidonate metabolites

Mairead A. Carroll, Monica K. Cheng, Elvira L. Liclican, Jing Li, Anabel B. Doumad, John C. McGiff

New York Medical College, Department of Pharmacology, Valhalla, New York 10595, USA

Correspondence: Mairead A. Carroll, e-mail: Mairead_Carroll@NYMC.edu

Abstract:
Cytochrome P450 (CYP)-dependent epoxyeicosatrienoic acids (EETs) dilate rat preglomerular microvessels (PGMVs) when adenosine 2A receptors (A2AR) are stimulated. As high salt intake increases epoxygenase activity and adenosine levels, we hypothesized that renal adenosine responses would be greater in high salt-fed rats. We have obtained evidence supporting this hypothesis in rats fed a high salt diet for 7 days. Stimulation of adenosine receptors with 2-chloroadenosine in kidneys obtained from rats on high salt (4%) intake produced an increase in EET release that was several-fold greater than in kidneys of rats on normal salt (0.4% NaCl) diets, which was associated with a sharp decline in renovascular resistance. Under conditions of high salt intake, an associated upregulation of A2AR and 2C23 protein expression was observed. As EETs are renal vasodilator and natriuretic eicosanoids, the antipressor response to salt loading may operate through an A2AR – EET mechanism. These findings expand the role of adenosine-related mechanisms in protecting renal function.

Key words: kidney, EETs, adenosine 2A receptors, salt


Purinoceptors (P) are classified as either P1 or P2 according to their endogenous agonists: ATP (P2) and its hydrolysis product, adenosine (P1). They are found in the renal microcirculation in relative abundance [6, 12]. Purinoceptors in preglomerular microvessels (PGMVs) are linked to activation of cytochrome P450 monooxygenase-derived arachidonic acid (CYP-AA) metabolism: 1) ω-hydroxylase is coupled to the P2X receptor with production of 20-hydroxyeicosatetraenoic acid (20-HETE) [16]; and 2) epoxygenases (mainly the 2C23 isoform) is coupled to the adenosine 2A receptor (A2AR) with production of epoxyeicosatrienoic acids (EETs) [2]. A dynamic and antagonistic interaction between EETs and 20-HETE has been identified in PGMVs and is evident in their independent and opposing actions on autoregulation of renal blood flow [5]. Thus, the constrictor response of PGMVs to elevation of blood pressure (the signature of renal autoregulation), which maintains renal blood flow at a constant level, can be abolished by inhibiting