Localization and Regulation of Renal Receptors for Angiotensin II and Atrial Natriuretic Peptide

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Sexton, P.M., Zhuo, J. and Mendelsohn, F.A.O. Localization and Regulation of Renal Receptors for Angiotensin II and Atrial Natriuretic Peptide. Tohoku J. Exp. Med., 1992, 166 (1), 41-56 —— The anatomical distribution of receptors for angiotensin II (Ang II) and atrial natriuretic peptide (ANP) within the kidney has been investigated by in vitro autoradiography. Ang II and ANP receptor binding occurs together in several sites in the kidney, including renal vasculature, glomeruli, proximal convoluted tubule of the outer cortex, and the vasa recta bundles of the inner stripe of the outer medulla. However, in the glomeruli, Ang II receptor binding occurs predominantly in mesangial cells, while ANP receptors are localized mainly to the visceral epithelial cells. In the inner medulla, there is a moderate density of ANP receptors in marked contrast with Ang II binding which is not detected in this site. Both Ang II and ANP receptors are modulated by alterations in sodium and fluid intake, and the peptides themselves. The overlapping distribution of receptors for these two peptide hormones in several intrarenal sites may provide an anatomical basis for their physiological interaction to regulate renal hemodynamics and tubular reabsorption of sodium and water. —— kidney; angiotensin II; atrial natriuretic peptide; receptor; autoradiography

Angiotensin II (Ang II) and atrial natriuretic peptide (ANP) are two major hormonal systems which play an important role in regulation of systemic arterial blood pressure and maintenance of body salt and fluid homeostasis. In the kidney, there are similarities in intrarenal distribution of Ang II and ANP receptors, but these two peptides appear to exert opposite influences on renal hemodynamics and tubular transport. Ang II acts on renal vasculature to decrease renal blood flow (RBF), glomerular filtration rate (GFR), and ultrafiltration coefficient (Kf). Ang II exerts its sodium retaining effect through direct stimulation of proximal tubular reabsorption of sodium, and indirectly

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enhancing distal sodium reabsorption mediated by aldosterone. By contrast, ANP causes renal vasodilation and increases RBF, GFR and Kf. In addition, ANP inhibits tubular reabsorption of sodium and water in most, if not all, segments of renal tubule to promote urinary sodium and water excretion. This paper reviews the localization and regulation of renal receptors for these two peptides and relates overlapping distribution of their receptors to their physiological interactions within the kidney.

Renal actions of Ang II

Ang II exerts multiple actions in the kidney including regulation of renal hemodynamics (Navar et al. 1986; Blantz and Gabbai 1987; Mitchell and Navar 1991), inhibition of renin synthesis and release (Davis and Freeman 1976), and stimulation of proximal tubular transport of sodium (Schuster et al. 1984; Harris and Navar 1985; Wang and Chan 1990). Ang II is a potent renal vasoconstrictor and may alter RBF and GFR by direct constriction of both pre- and postglomerular arterioles (Navar et al. 1986; Steinhausen et al. 1986), as well as direct contraction of glomerular mesangium to influence Kf and intraglomerular hemodynamics (Ausiello et al. 1980; Blantz and Gabbai 1987). In the proximal nephron, Ang II displays biphasic actions on sodium transport with direct stimulation at physiological concentrations and inhibition at higher concentrations (Harris and Young 1977; Schuster et al. 1984; Wang and Chan 1990). Moreover, Ang II promotes bicarbonate reabsorption and acidification of proximal tubular fluid (Liu and Cogan 1987; Geibel et al. 1990), stimulates gluconeogenesis (Guder 1979) and stimulates the growth of proximal tubular cells (Norman 1991). These proximal effects are necessary for maintenance of proximal glomerulotubular balance (Harris et al. 1987a; Zhuo et al. 1989). In addition, Ang II appears to be important in the regulation of medullary blood flow (Chou et al. 1986) but its distal tubular effects are currently unclear.

Renal actions of atrial natriuretic peptide

In the kidney, ANP causes marked diuresis and natriuresis (for details see reviews Harris and Skinner 1990; Cogan 1990; Zeidel 1990). The mechanisms whereby ANP induces dramatic increases in urinary excretion of sodium and water remain an issue of controversy. These diuretic and natriuretic effects of ANP are thought to be mediated by ANP-induced alterations in renal hemodynamics (Cogan 1990). Decrease in renal perfusion pressure markedly attenuates ANP-induced natriuresis (Seymour et al. 1987), while Ang II-mediated increments in perfusion pressure augment this action (Mandez et al. 1986). At the glomerulus, ANP dilates the afferent arteriole and probably constricts the efferent arteriole (Marin-Grez et al. 1986), consequently resulting in glomerular hyperfiltration and increased filtration fraction. These changes in renal hemodynamics are a primary cause for ANP-induced natriuresis (Cogan 1990).
However, at low concentrations of ANP, natriuresis can still occur without detectable increments in filtered load (Burnett et al. 1986; Banks 1988). This may be associated with either redistribution of blood flow from superficial to juxtamedullary nephrons (Borenstein et al. 1983), or inhibition of tubular transport of sodium and water.

Like Ang II, ANP also has multiple sites of action on renal tubular sodium reabsorption. It is now clear that ANP inhibits sodium reabsorption in the medullary collecting duct (Zeidel 1990). ANP antagonizes Ang II-induced sodium transport in the proximal tubule (Harris et al. 1987b; Garvin 1989). Although, whether ANP has a direct action in the proximal tubule is still controversial (Baum and Toto 1986; Cogan 1990). This intrarenal interaction between Ang II and ANP may contribute to the impairment of proximal glomerulo-tubular balance seen during infusion of ANP alone (Zhuo et al. 1989; Harris and Skinner 1990). However, ANP does not have any effect on the loop of Henle (Kondo et al. 1986).

In vitro autoradiographic localization of intrarenal receptors for Ang II and ANP

To clarify renal actions of these hormones, we have used quantitative in vitro autoradiography to localize renal Ang II and ANP binding sites. For Ang II receptors the radioligand was either the superagonist analogue, $^{125}$I-[Sar1]Ang II (Mendelsohn et al. 1983), or later the antagonist analogue, $^{125}$I-[Sar1, Ile8] Ang II. For ANP localization, $^{125}$I-rat ANP (1–28) was used as radioligand (Chai et al. 1986). To map the renal receptors for these two peptides, unfixed, slide-mounted cryostat sections (20 μm thickness) were incubated under equilibrium conditions with the radioligands and then rapidly washed with ice-cold buffer to remove non-specifically bound radioligand, and exposed to x-ray film (Chai et al. 1986; Mendelsohn et al. 1986). The resulting autoradiographs were analysed by computerized densitometry (MCID, Imaging Research Inc., Canada).

Distribution of Ang II receptors in the kidney

In the rat kidney, a striking pattern of distribution of Ang II receptor binding is seen in renal cortex and medulla (Mendelsohn et al. 1983, 1986, 1987a). In the outer cortex, a very high density of binding occurs over glomeruli with a density gradient of superficial over juxtamedullary nephrons (Mendelsohn et al. 1986), and low to moderate binding is seen over the intervening outer cortex associated with proximal convoluted tubule. In the medulla, a very high density of binding is found over longitudinal bands tranversing the inner stripe of the outer medulla, and these bands correspond to the vasa recta bundles (Mendelsohn et al. 1987a). There is also a moderate density of Ang II receptor binding in the interbundle area of the inner stripe of the outer medulla. However, Ang II receptor binding in the outer stripe is undetectable. In addition, Ang II receptor binding associated with the vasa recta bundles continues into the inner medulla.
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but dissipates toward the tip, as do the bundles themselves. Ang II receptor binding is also seen overlying the media of some large blood vessels and over the muscular layer of the pelvic expansion of the ureter, but it is of much lower density than the binding associated with glomeruli, proximal convoluted tubule, and the vasa recta bundles (Mendelsohn et al. 1987a).

A similar, but not identical distribution of Ang II receptors occurs in the cynomologus monkey kidney (Mendelsohn et al. 1987b) As in the rat, Ang II receptors are highly concentrated in glomeruli throughout the renal cortex. In addition, moderate homogenous labelling occurs in the outer and inner cortex. Unlike the very high Ang II receptors concentration in the outer medulla of rat kidney, binding in the monkey renal medulla is only moderate, and confined to radiating bands in the outer two-thirds of the medulla, a pattern consistent with localization over the vasa recta bundles. No binding was present in the inner zone of the medulla.

In the human kidney, dense binding is observed over glomeruli as well as the outer medulla although little binding is found in the cortex between the glomeruli (Fig. 1). As in the other species, the outer medullary binding is most dense over vasa recta bundles but also includes moderate binding throughout the outer medulla (Yamada et al. 1990).

Renal Ang II receptor subtypes

Renal Ang II receptor subtypes have been proposed in many previous radioligand-receptor binding studies (for review see Douglas 1987a, b, c). Recent development of specific peptide and nonpeptide Ang II receptor antagonists has allowed differentiation of Ang II receptor into two subtypes: type 1 (AT-1) and type 2 (AT-2); or type B and type A, respectively (for review see Peach and Dostal 1990). The non-peptide antagonist, DuP 753, exhibits approximate 1000-fold greater affinity for AT-1 receptors than AT-2 antagonists, PD 123177 or CGP 42112A. For AT-2 receptors, however, PD 123177 and CGP 42112A show 1000-fold greater affinity than the AT-1 antagonist, DuP 753. Accordingly, AT-1 receptors are determined in the presence of excess concentrations of the AT-2 antagonist, PD 123177, while AT-2 receptors are localized in the presence of excess concentrations of the AT-1 antagonist, DuP 753.

Renal Ang II receptor subtypes have not been fully investigated. However, a preliminary report has shown that the non-peptide antagonist, EX89, which has

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Fig. 1. Darkfield localization of receptors for Ang II in the human kidney* with 125I-\textsuperscript{[Sar\textsubscript{1},Ile\textsubscript{8}]Ang II. A) Total binding (×5), B) Binding in the presence of 1 μM unlabelled Ang II (×5), C) Corresponding haemotoxylin and eosin stained section to the autoradiograph in D (×12), D) Higher magnification of the binding to the medulla (×12). Abbreviations: Cx, cortex; OM, outer medulla; bv, blood vessel; VRB, vasa recta bundle; G, glomeruli.

*Histologically normal tissue adjacent to renal cell carcinoma removed at operation.
high affinity for AT-1 binding sites, potently blocked $^{125}$I-[Sar1]Ang II binding in all regions of rat kidney, including glomeruli, proximal convoluted tubule, and vasa recta bundles, whereas CGP 42112A had little effect (Gasparo et al. 1990). This indicates that renal Ang II receptors are AT-1 subtype. We have recently confirmed this finding (Zhuo, Song, Harris and Mendelsohn, submitted). However, it is still possible that there is a small population of AT-2 receptors in the kidney.

**Functional significance of renal Ang II receptors**

The high density of Ang II receptor binding associated with glomeruli appears to be localized to mesangial cells (Bianchi et al. 1986). This suggestion is supported by localization of autoradiographic grains to the mesangium following in vivo administration of radiolabelled Ang II (Osborne et al. 1975; Bianchi et al. 1986), by the contractile response of glomeruli to Ang II in vitro (Ausiello et al. 1980), and by the presence of Ang II binding sites in cultured mesangial cells (Foidart et al. 1980). The distribution of specific, high affinity Ang II receptors to the glomerular mesangium is of physiological significance, as contraction of the mesangium would reduce the available ultrafiltration surface area and glomerular membrane hydraulic conductance, with a consequent fall in ultrafiltration coefficient ($k_f$) and intraglomerular plasma flow (Ichikawa and Brenner 1984). The action of Ang II on glomerular mesangial cells is likely to be mediated by the Ang II-stimulated inositol phosphate formation (Sekar et al. 1990), and the latter effect can be blocked by the AT-1 receptor antagonist, EX89 (Pfeilschifter 1990). Inositol triphosphate (IP3) has been shown to increase intracellular concentration of ionized calcium (Bonventre et al. 1985) which activates the calcium binding protein, calmodulin, thus causing contraction of the glomerular mesangium (Sekar et al. 1990).

Ang II receptors in proximal convoluted tubule are associated with both basolateral and apical brush border membrane (for review see Douglas 1987a). Proximal convoluted tubules possess the highest density of Ang II receptor binding sites when compared with any other tubular segments (Mujais et al. 1986). This is of functional importance since sodium and water reabsorption account for 70% of glomerular filtered load. Ang II has multiple actions on this tubular segment, including stimulation of sodium (Harris and Navar 1985), bicarbonate reabsorption (Liu and Cogan 1987), gluconeogenesis (Guder 1979), and the growth of proximal tubular cells (Norman 1991). Although the action of Ang II on sodium transport involves the AT-1 receptor subtype (Xie et al. 1990), and suppression of cAMP production (Liu and Cogan 1989), activation of calcium channels (Douglas et al. 1990), or arachidonate metabolism by P450 enzymes (Romero et al. 1991), the AII receptor subtype and cellular signal transduction mechanisms responsible for other proximal actions of Ang II remain to be elucidated.
The cellular localization of the abundant Ang II receptors associated with the inner stripe of the outer medulla is still to be established. Receptors occur diffusely throughout the inner stripe and are in highest density in the region of the vasa recta bundles.

**Regulation of renal Ang II receptors**

Glomerular Ang II receptors undergo regulatory changes during altered NaCl intake (Douglas 1987b). Ang II receptor numbers increase during NaCl loading and fall during low NaCl intake (Beaufils et al. 1976; Skorecki et al. 1983; Bellucci and Wilkes 1984). The latter effect can be reproduced by Ang II infusion, and blocked by the angiotensin converting enzyme inhibitor, captopril, suggesting that Ang II is responsible for down-regulation of its receptors in glomeruli (Bellucci and Wilkes 1984; Wilkes et al. 1988).

In addition, glomerular Ang II receptors are also influenced by several heterologous hormones, being depressed by both corticosteroids and oestrogen (Douglas 1987b, c), and enhanced by prolactin (Douglas 1987b). Rats with streptozotocin-induced diabetes have less glomerular Ang II receptors and this effect is corrected by insulin administration (Ballermann et al. 1984; Wilkes 1987). Increased glomerular Ang II receptors have been reported in young spontaneously hypertensive rats (Brasier et al. 1984), DOCA-treated rats (Wilson et al. 1989) and rats with renal denervation (Wilkes et al. 1988).

The properties and regulation of proximal tubular Ang II receptors differ from those of glomerular receptors. NaCl loading downregulates tubular receptors in sharp contrast to the glomerular counterparts (Douglas 1987a). The tubular receptors are also of lower affinity and differ in ligand specificity (Douglas 1987a). Interestingly, the Ang II receptors on the apical brush border membranes are increased by transmembrane potential difference (Brown and Douglas 1987).

**Distribution of ANP receptors in kidney**

In vitro autoradiographic studies conducted in this laboratory have revealed that in rat kidney ANP receptor binding occurs in both the cortex and medulla (Chai et al. 1986; Mendelsohn et al. 1987b). In the cortex, high density binding is mainly associated with glomeruli with a moderate density of binding in the outer cortex, corresponding to the interglomerular area - proximal convoluted tubule. In the inner stripe of outer medulla, moderate binding is associated with vasa recta bundles with diffuse low density of binding in the interbundle zones. The inner medulla contains a high density of ANP receptors and this binding has been further localized to inner medullary collecting ducts (Koseki et al. 1986).

The intrarenal distribution of ANP receptors appears to be well conserved with similar localization reported for rat (Chai et al. 1986), guinea pig and human kidney (Mantyh et al. 1986). However, the cellular localization of ANP receptors in the glomeruli is still controversial. Using separate cultures of glomerular...
mesangial and epithelial cells, Ballermann and colleagues (1985) demonstrated specific binding of ANP to mesangial but not epithelial cells, suggesting that the binding seen in the glomeruli as revealed by in vitro autoradiography is predominantly associated with mesangium. However, studies by electron microscopic autoradiography indicate that unlike Ang II receptors, ANP receptors in glomeruli are predominantly localized to the visceral epithelial cells, although radiolabelled ANP is also found to bind to the mesangial cells (Bianchi et al. 1986).

In the renal tubule, ANP receptors are mainly distributed to the segments of proximal tubule in the outer cortex and inner medullary collecting ducts (Chai et al. 1986; Healy and Fanestil 1986; Yamamoto et al. 1987), with distal tubule and cortical thick ascending limb of the loop of Henle devoid of binding. Using quantitative in vitro autoradiography, we constructed binding isotherms of the competition for $^{125}$I-ANP binding in the proximal tubule with unlabelled ANP (1–28). Analysis of this data using the LIGAND Program (Munson and Rodbard

![Graph A](image)

![Graph B](image)

Fig. 2. A. Binding isotherm of the competition for $^{125}$I-ANP (1–28) binding, to proximal tubule by unlabelled ANP (1–28). The broken lines represent 95% confidence limits. B. Scatchard plot of the data.
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1980) indicates the existence of a high affinity site and a second low affinity site of borderline significance \( p = 0.06 \) with dissociation constants of \( 1.15 \pm 0.26 \text{ nM} \) and \( 3.5 \pm 6.4 \text{ nM} \), respectively, and binding site concentrations of \( 52 \pm 12 \text{ fmol/mg protein} \) and \( 2.0 \pm 4.0 \text{ pmol/mg protein} \), respectively (Fig. 2). The second, low affinity binding sites may be associated with degradation sites, while the high affinity binding sites have a similar affinity constant to those we reported for both the inner medulla and glomerulus under similar experimental conditions, as shown in Table 1 (Chai et al. 1986; Tsunoda et al. 1988).

The anatomical distribution of ANP receptors is similar to the reported distribution of ANP-sensitive guanylate cyclase along the nephron (Table 2, Nonoguchi et al. 1987), and suggests that activation of guanylate cyclase may be

<p>| Table 1. Comparison of the distribution of receptors for ANP and ANP-sensitive cyclic GMP production in the rat kidney |</p>
<table>
<thead>
<tr>
<th>Renal structure</th>
<th>cGMP stimulation</th>
<th>Receptor density</th>
</tr>
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<tbody>
<tr>
<td>Glomerulus</td>
<td># (^b)</td>
<td>#</td>
</tr>
<tr>
<td>Proximal convoluted tubule</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Proximal straight tubule (s-2)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Proximal straight tubule</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Thin descending limb</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Thin limb (IM) (? vasa recta)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Medullary thick ascending limb</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Vasa recta (OM)</td>
<td>ND (^c)</td>
<td>#</td>
</tr>
<tr>
<td>Cortical thick ascending limb</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Distal tubule</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cortical collecting duct</td>
<td>+</td>
<td>ND</td>
</tr>
<tr>
<td>Outer medullary collecting duct</td>
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<td>ND</td>
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<tr>
<td>Inner medullary collecting duct</td>
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\(^a\)Adapted from Nonoguchi et al. (1987)
\(^b\) + ~ #, relative cGMP stimulation or receptor density.
\(^c\)ND, not determined.

<p>| Table 2. Comparison of affinities for renal ANP binding sites as determined by quantitative in vitro autoradiography |</p>
<table>
<thead>
<tr>
<th>Renal binding site</th>
<th>Affinity</th>
</tr>
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<tbody>
<tr>
<td>Glomerulus(^a)</td>
<td>(0.48 \pm 0.06 \times 10^9 \text{ M}^{-1})</td>
</tr>
<tr>
<td>Proximal tubule</td>
<td>(1.15 \pm 0.26 \times 10^9 \text{ M}^{-1})</td>
</tr>
<tr>
<td></td>
<td>(3.5 \pm 6.4 \times 10^8 \text{ M}^{-1})</td>
</tr>
<tr>
<td>Inner medulla(^a) (collecting duct)</td>
<td>(0.93 \pm 0.22 \times 10^9 \text{ M}^{-1})</td>
</tr>
</tbody>
</table>

\(^a\)From Chai et al. (1986)
\(^b\)Low affinity site.
one important signal transduction mechanism for the renal hemodynamic and tubular actions of ANP.

Renal ANP clearance receptors

Recent studies on structure-activity relationships, and ligand-receptor competition, suggest the existence of ANP receptor subtypes in the kidney (Maack et al. 1987; Pandey et al. 1988; Almeida et al. 1989; Bovy et al. 1989). In addition to the ANP receptors described above, recent work has shown that the C-ANF (4-23) analogue of ANP binds with high affinity to the majority of native ANP binding sites in the renal cortex and isolated glomeruli (Maack et al. 1987). However, these ANP binding sites do not mediate the known ANP-induced increase in guanosine 5'-cyclic monophosphate (cGMP) in cultured glomerular mesangial cells or renal effects of ANP on vasculature, glomerular hemodynamics and urinary sodium excretion in isolated perfused rat kidney. This second class of ANP receptors, termed clearance receptors, is biologically silent and may serve as clearance binding sites for the hormone (Maack et al. 1987; Almeida et al. 1989). The physiological significance of clearance receptors is not fully understood at present, but they may act to modulate endogenous plasma ANP concentration (Maack et al. 1987; Seymour et al. 1991).

Regulation of renal ANP receptors

Renal ANP receptors show an ontogenic developmental pattern. The numbers of receptors in glomeruli and inner medullary collecting ducts are low after birth but rise progressively to the 5th week of postnatal life (Semmekrot et al. 1990). There is no difference in the ontogenic developmental patterns of renal ANP receptor binding between spontaneously hypertensive and Wistar-Kyoto normotensive rats (Ogura et al. 1989).

Renal ANP receptors are modulated in many states of altered salt and fluid homeostasis. In isolated glomeruli, ANP receptor density increases in response to chronic water deprivation (Lynch et al. 1986; Gauguelin et al. 1988) and low sodium diet, and decreases with high sodium intake (Ballermann et al. 1985; Lynch et al. 1986; Gauguelin et al. 1988).

ANP receptor binding in the kidney is also influenced during pathophysiological states. For instance, in a model of chronic heart failure secondary to healed myocardial infarction in this laboratory, ANP receptors in the inner medulla were down-regulated in proportion to the degree of heart failure and inversely correlated to plasma ANP levels (Tsunoda et al. 1988). Similar, selective down-regulation of renal inner medullary ANP receptors has also been observed in spontaneously hypertensive rats (Agnati et al. 1988). Down-regulation of renal ANP receptors may contribute to the impaired sodium and water excretion and the blunted natriuretic response to ANP in these disorders. Furthermore, increased glomerular ANP receptors have been reported in rats
treated with DOCA or dexamethasone (Lynch et al. 1986; Yamamoto et al. 1987), whereas decreased glomerular ANP receptors were seen in streptozotocin diabetes (Lynch et al. 1986) and in one kidney, I clip hypertensive rats (Garcia et al. 1988). The mechanisms underlying these changes in renal receptors for ANP remain to be investigated.

The neutral endopeptidase 24.11 (NEP) cleaves ANP to produce an inactive open-ring metabolite (Seymour et al. 1991). This therefore represents another pathway for ANP degradation, in parallel with renal clearance receptors. Indeed, blockade of both clearance receptors by C-ANP (4-23) and NEP by SQ 28,603 leads to an additive effect on plasma ANP levels and renal excretion of cyclic GMP (Seymour et al. 1991).

**Overlapping distribution of renal receptors for Ang II and ANP and their physiological interaction**

Although Ang II and ANP do not directly compete at their respective binding sites (Chai et al. 1986; Bianchi et al. 1986), our receptor mapping studies have revealed that Ang II and ANP binding in the rat kidney are closely juxtaposed in several anatomical sites, including the renal vasculature, glomeruli, proximal convoluted tubule and the inner stripe of the outer medulla (Mendelsohn et al. 1986, 1987b). Such overlapping distribution of renal receptors for Ang II and ANP in the same structures raises the possibility that these two peptides might interact physiologically. Indeed, recent evidence indicates that Ang II and ANP do have opposite actions on multiple intrarenal sites (Harris and Skinner 1990). In glomeruli, Ang II acts as a vasoconstrictor to decrease RBF, GFR and Kf (Ichikawa and Brenner 1984; Navar et al. 1986; Blantz and Gabbai 1987), while ANP causes mainly afferent vasodilatation and increases glomerular capillary permeability (Cogan 1990; Zeidel 1990). In the proximal nephron, ANP has been shown to inhibit the Ang II-stimulated sodium transport (Harris et al. 1987b; Garvin 1989) and to disrupt proximal glomerulo-tubular balance (Zhao et al. 1989). Similarly, Ang II decreases vasa recta and papillary blood flow in the renal medulla (Chou et al. 1986), whereas ANP has the opposite effect (Ballermann and Brenner 1987). These physiological interactions between Ang II and ANP in the kidney parallel those demonstrated in other target organs including systemic vasculature, adrenal gland, and the central nervous system. By acting on intrarenal sites and extrarenal tissues separately or in combination, Ang II and ANP are important humoral factors in the regulation of systemic arterial blood pressure, body fluid and electrolyte homeostasis.

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References


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