

学位論文の内容の要旨

専攻	分子情報制御医学	部門	生体情報学
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論文題目	Effects of the novel nonsteroidal mineralocorticoid receptor blocker, esaxerenone (CS-3150), on blood pressure and urinary angiotensinogen in low-renin Dahl salt-sensitive hypertensive rats		
(論文要旨)			
<p>Abstract</p> <p>Herein, we studied the effects of the novel nonsteroidal selective mineralocorticoid receptor (MR) blocker, esaxerenone, on blood pressure and renal injury in Dahl salt-sensitive (DSS) rats. We also monitored the urinary intact and total angiotensinogen (AGT). DSS rats were given a normal salt diet (NS: 0.4% NaCl, n = 10), high salt diet (HS: 8% NaCl, n = 10), HS + esaxerenone (1 mg/kg/day, p. o., n = 10), or HS + losartan (angiotensin II receptor blocker, 10 mg/kg/day, p. o., n = 10) for 6 weeks. Glomerular and tubulointerstitial tissues were obtained by a laser capture method. HS-treated DSS rats developed hypertension, albuminuria and glomerular injury, which were associated with increased glomerular desmin staining and reduced mRNA levels of glomerular podocin and nephrin. HS-treated DSS rats also showed tubulointerstitial fibrosis with an increase in renal oxidative stress (4-hydroxynonenal staining). The urinary (total AGT - intact AGT)/intact AGT ratio, an indicator of intrarenal renin activity, was significantly suppressed in HS-treated DSS rats. Treatment with esaxerenone significantly decreased blood pressure, while losartan did not. Furthermore, esaxerenone attenuated the development of albuminuria, glomerular injury and tubulointerstitial fibrosis more than losartan did, and this was associated with reduced renal oxidative stress. These data indicate that esaxerenone induces antihypertensive and renal protective effects in salt-dependent hypertensive subjects with suppressed intrarenal renin activity, as indicated by low levels of the urinary (total AGT - intact-AGT)/intact AGT ratio.</p>			

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