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LETTER

Inhibition of Renal Fibrosis and Glomerular Injury by Sacubitril/Valsartan, a Combination Angiotensin Receptor Blocker and Neprilysin Inhibitor, in a Salt-Sensitive Hypertensive Model Using Angiotensin 1 Receptor Knockout Mice: The Contribution of Non-Angiotensin Blocking Effects to Renal Protection

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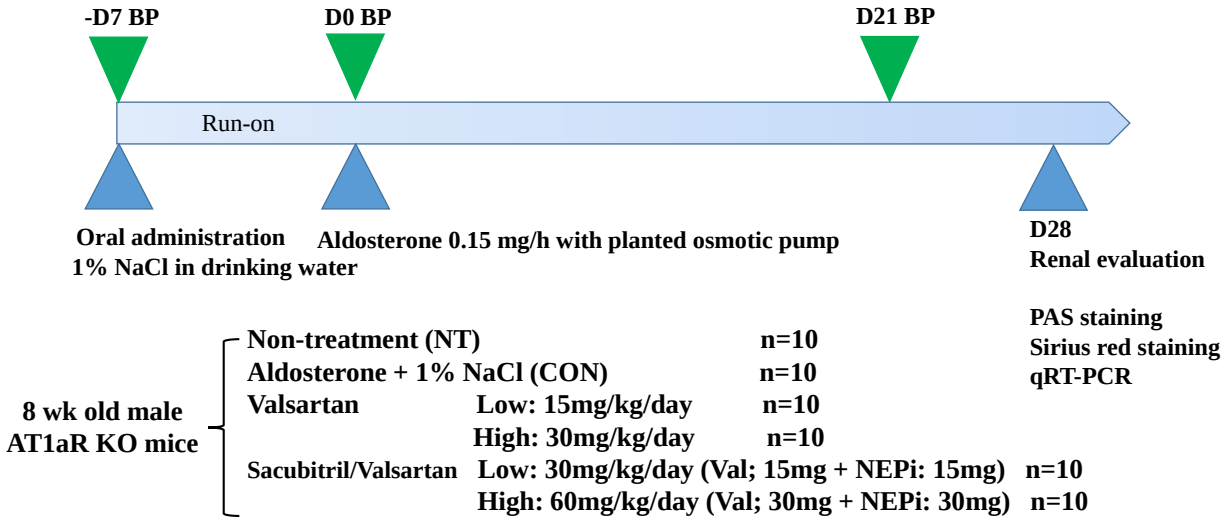

Supplementry 1. Study Protocol.
Mice were divided into 6 groups: (1) Nontreatment; (2) aldosterone (0.15 μg/h) + 1 % NaCl treatment; (3) valsartan low, aldosterone (0.15 μg/h) + 1 % NaCl + valsartan (15 mg/kg per day) treatment; (4) valsartan high, aldosterone (0.15 μg/h) + 1 % NaCl and valsartan (30 mg/kg per day) treatment; (5) Sac/Val, aldosterone (0.15 μg/h) + 1 % NaCl + Sac/Val (30 mg/kg per day, Sac/Val 30 mg=valsartan 15 mg + NEPi 15 mg) treatment; and (6) Sac/Val high, aldosterone (0.15 μg/h) + 1 % NaCl + Sac/Val (60 mg/kg per day, Sac/Val 60 mg=valsartan 30 mg + NEPi 30 mg) treatment. Each group contained 10 mice.

We started an oral administration of Sac/Val (30-60 mg/kg/day) and valsartan (as a control group) (15-30 mg/kg/day) 7 days before administration of aldosterone and 1 % NaCl. Then, we prepared an aldosterone-sustained administration model using an osmotic pump, implanted all of the mice 7 days later and used an experimental system to approximate the aldosterone breakthrough model.