Angiotensin 1-7protects against angiotensin II-induced endoplasmic reticulum stress and endothelial dysfunction via Mas receptor

Angiotensin 1-7 (Ang 1-7) counter-regulates the cardiovascular actions of angiotensin II (Ang II) (1). The present study investigated the protective effect of Ang 1-7 against Ang II-induced endoplasmic reticulum (ER) stress and endothelial dysfunction. Vascular reactivity in mouse aortae was evaluated by wire myograph.The effects of Ang 1-7 on Ang II-induced ER stress markers, nitric oxide activity and generation in the mouse aortas and HUVECs were assessed by western blot and 4-amino-5-methylamino-2',7'-difluorofluorescein (DAF-DA, 1 μM), respectively. *Ex vivo* treatment with Ang II (0.5 μM, 24 hours) impaired endothelium-dependent relaxation in mouse aortas; this harmful effect of Ang II was reversed byco-treatment with ER stress inhibitors, l4-phenylbutyric acid (PBA) and tauroursodeoxycholic acid (TUDCA) as well as Ang 1-7 (Fig 1). The Mas receptor antagonist, A779 antagonized the effect of Ang 1-7. The elevated mRNA expression of CHOP, Grp78 and ATF4 or protein expression of p-EIF2α and ATF6 (ER stress markers) in Ang II-treated mouse aortas were blunted by co-treatment with Ang 1-7 and the latter effect was reversed by A779 (Fig 2). Furthermore, Ang II-induced reduction in botheNOS phosphorylation and NO production was inhibited by Ang 1-7.The present study provides new evidence for functional antagonism between the two arms of the renin-angiotensin system in endothelial cells by demonstrating that Ang 1-7 ameliorates Ang II-stimulated ER stress to raise NO bioavailability, and subsequently preserves endothelial function.
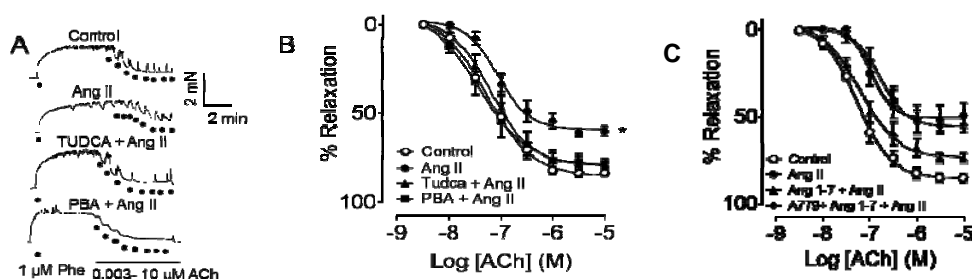

Fig 1. ER stress inhibitors (A and B) and Ang 1-7 (C) reversed Ang II-induced impaired of Ach-induced relaxation
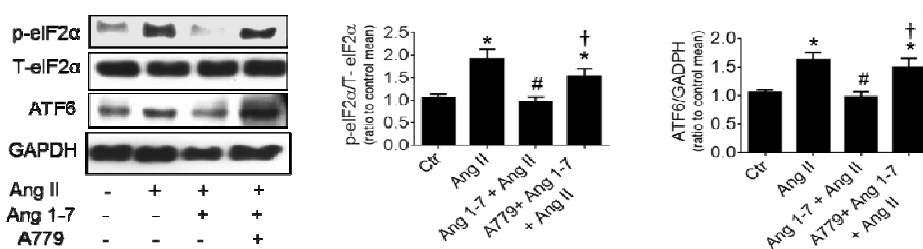

Fig 2. Ang 1-7 decreased Ang II stimulated ER stress

Reference:

(1) Galan *et al.*, (2014). Biochim. BiophysActa 1843: 1063-75