

[課程－2]

審査の結果の要旨

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In this study, I investigate the mechanism of vascular dysfunction in the development of salt sensitive hypertension. I used low dose N-nitro-L-arginine Methyl Ester (L-NAME) inhibit nitric oxide (NO) synthesis to induce mildly vascular dysfunction. The results are like this:

1. L-NAME caused salt-sensitive hypertension in rodent model.
2. Non-pressure dose L-NAME didn't induce any severe fibrotic changes in the kidney.
3. NCC was activated in this L-NAME-induced salt-sensitive hypertension but not ENaC in 8-week-old C57/B6j mice.
4. After knock-out NCC, L-NAME failed to induce salt-sensitive hypertension.
5. NO inhibited NCC in mDCT cells (mouse kidney distal tubule cell), which confirmed by both NO inhibitor and donor.
6. Oxidative stress played a role in NO-induced inhibition of NCC in mDCT cells via p-SPAK pathway.

7. TEMPO attenuated the L-NAME-induced increases in superoxide, MBP and p-NCC expression in the C57BL/6J mice.

In the present study, systemic inhibition of NO induced salt-sensitive hypertension via oxidative stress/p-SPAK pathway. Those data could be translated into pathophysiology of aged or diabetes who show salt-sensitive hypertension, which is conceivable to deserve a PhD. degree award.