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Local aldosterone synthesis in mouse colon: Discovery of the components of aldosterone synthesis, enzyme activation and its stimulation

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Background: Aldosterone (Aldo) is the principal mineralocorticoid hormone mainly produced in adrenal gland. It regulates blood pressure, plasma sodium and potassium levels via its renal effects. It can be synthesized not only in the adrenal gland but also in other tissues, e.g. brain, skin, blood vessels, heart, and kidney. Intestine maintains the homeostasis of fluid and electrolyte in addition to kidney. We have earlier described the presence of renin-angiotensin system in the large intestine and a precursor of Aldo, corticosterone. In colon, Aldo promotes sodium, potassium and water exchange. Then, the question is whether colon, the important regulator of water and electrolyte balance, is able to locally produce Aldo and if so, how its local synthesis is regulated.

Materials & Methods: Mouse colon samples were used for the detection of Aldo and Aldo synthase (CYP11B2), the enzyme to produce Aldo, at gene and protein levels. Enzymatic reaction measuring the enzymatic activity was set to investigate whether CYP11B2 enzyme is in active form in colon. Angiotensin (Ang) peptides, cAMP (second messenger of ACTH) in ex vivo incubation and different dietary sodium intake were used to investigate whether the Aldo synthesis in colon is stimulated by the same stimulatory factors as in adrenal gland.

Results: The whole chain of Aldo synthesis from the gene and protein of CYP11B2 to the final product, Aldo, was found in mouse colon. CYP11B2 enzyme protein in colon is in active form to utilize precursor to produce Aldo. Ang I, Ang II, Ang III, cAMP and dietary low-sodium intake are able to stimulate Aldo synthesis in mouse colon.

Conclusion & Significance: Mouse colon is able to locally synthesize Aldo. The colonic Aldo synthesis is stimulated by the same factors as in adrenal gland. This preclinical study raises question on clinical and possibly also therapeutic relevance of the findings.

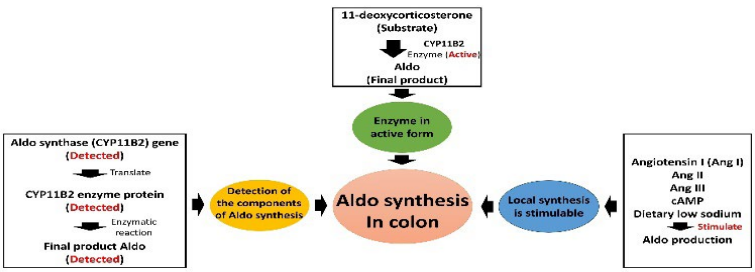

Figure 1. Local aldosterone (Aldo) synthesis in mouse colon: the detection of the components of Aldo synthesis, the enzyme in active form and its stimulation.

Recent Publications:

1. Pang Z, Korpela R, Vapaatalo H (2022) Intestinal aldosterone synthase activity and aldosterone synthesis in mouse. *J Physiol Pharmacol* 73: 503-512.
2. Pang Z, Launonen H, Korpela R, Vapaatalo H (2022) Local aldosterone synthesis in the large intestine of mouse: An ex vivo incubation study. *J Int Med Res* 50: 1-18.
3. Launonen H, Pang Z, Linden J, Siltari A, Korpela R, Vapaatalo H (2021) Evidence for local aldosterone synthesis in the large intestine of the mouse. *J Physiol Pharmacol*, 72: 807-815.
4. Pang Z, Zhang Y, Liu L (2019) Identification and functional characterization of interferon-γ-inducible lysosomal thiol reductase (GILT) gene in common Chinese cuttlefish Sepiella japonica. *Fish & Shellfish Immun* 86: 627-634.
5. Pang Z, Lü Z, Wang M, Gong L, Liu B, Jiang L, Liu L (2019) Characterization, relative abundances of mRNA transcripts, and subcellular localization of two forms of membrane progestin receptors (mPRs) in the common Chinese cuttlefish, Sepiella japonica. *Anim Reprod Sci* 208: 106107.

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Biography

Zan Pang, MSc, 30, is a Chinese PhD student in Medical Nutrition Physiology Group, Department of Pharmacology, Faculty of Medicine, University of Helsinki. He published 8 research articles before PhD pursuit. He has published 3 research articles for PhD thesis. His fourth and the last manuscript for PhD thesis was submitted and is under peer review. He has given several oral talks and poster presentations in conferences, symposiums, and seminars. He received the award of "the best poster presentation" on RPU Science Day event organized by University of Helsinki. He is now preparing his PhD thesis and looking for the Postdoc position.