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Research focus

- Electrophysiology and molecular biology of renal and epithelial ion channels
- Channelopathies and molecular mechanisms of ion channel regulation
- Role of the epithelial sodium channel (ENaC) in renal salt handling and the pathogenesis of arterial hypertension
- ENaC regulation in the aldosterone sensitive distal nephron (ASDN)

A main research focus of the group of Prof. Korbmacher is the epithelial sodium channel (ENaC) which is a member of the ENaC/degenerin family of ion channels. ENaC is localized in the apical membrane of epithelial cells and is the rate limiting step for sodium absorption in epithelial tissues including the aldosterone-sensitive distal nephron (ASDN). Abnormal ENaC activation in the ASDN may cause sodium retention and arterial hypertension. ENaC is one of the key targets of aldosterone. However, the molecular mechanisms involved in ENaC regulation in the ASDN are highly complex [1] and include aldosterone-dependent and independent mechanisms [2]. For example ENaC activity can be stimulated by norepinephrine [3] which may contribute to the hypertensive effect of increased renal sympathetic activity. A unique feature of ENaC is its proteolytic activation which involves specific cleavage sites and the release of inhibitory peptide fragments. The physiologically relevant proteases involved in ENaC regulation remain to be identified [4, 5]. Moreover, it has to be determined how these proteases are regulated and linked to ENaC regulation by aldosterone. A better understanding of the mechanisms involved in ENaC regulation will hopefully provide novel insights into the physiology and pathophysiology of arterial hypertension. This ultimately may lead to new diagnostic and therapeutic concepts.

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2. Nesterov V, Dahlmann A, Krueger B, Bertog M, Loffing J, Korbmacher C (2012) Aldosterone-dependent and -independent regulation of the epithelial sodium channel (ENaC) in mouse distal nephron. Am J Physiol Renal Physiol 303: F1289-99 (PMID: 22933298)

3. Mansley MK, Neuhuber W, Korbmacher C, Bertog M (2015) Norepinephrine stimulates the epithelial Na^+ channel in cortical collecting duct cells via α_2-adrenoceptors. Am J Physiol Renal Physiol 308: F450-8 (PMID: 25520009)

4. Haerteis S, Krappitz M, Diakov A, Krappitz A, Rauh R, Korbmacher C. 2012. Plasmin and chymotrypsin have distinct preferences for channel activating cleavage sites in the γ subunit of the human epithelial sodium channel. J Gen Physiol 140: 375-89 (PMID: 22966015)

5. Haerteis S, Krappitz A, Krappitz M, Murphy JE, Bertog M, Krueger B, Nacken R, Chung H, Hollenberg MD, Knecht W, Bunnett NW, Korbmacher C (2014) Proteolytic activation of the human epithelial sodium channel by trypsin IV and trypsin I involves distinct cleavage sites. J Biol Chem 289: 19067-78 (PMID: 24841206)