

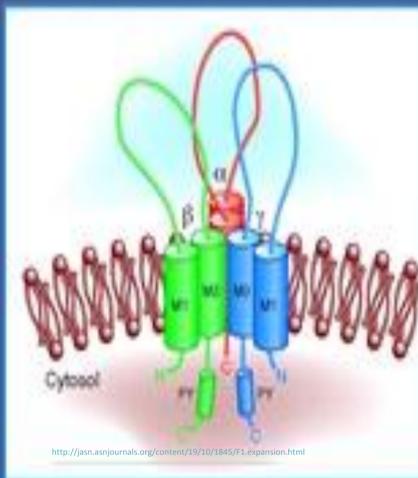


# Function of Epithelial Sodium Channel in The Heart

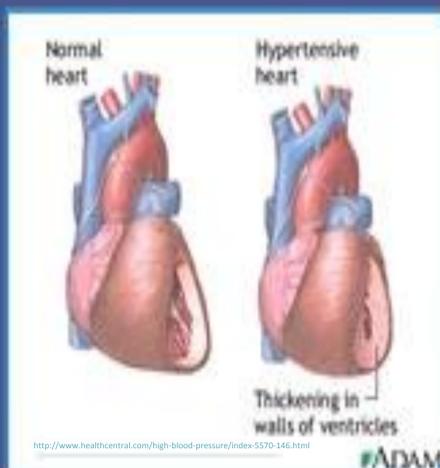


## Introduction:

- The Epithelial Sodium Channel (ENaC) is a trimeric protein found on the apical membrane of a variety of epithelia throughout the body.
- ENaC plays a role in regulating blood volume, by maintaining homeostatic Na<sup>+</sup> balance in the kidneys
- ENaC is activated by proteolytic cleavage of the  $\alpha$  and  $\gamma$  subunits at the extracellular loop[1]



- 1 in 3 adults in the United States has high blood pressure [2] and activation of ENaC increases BP.
- ENaC mediates sodium transport in non-renal epithelia, however, its expression and function in non-epithelial cells is poorly determined.
- We have detected widespread expression of the three ENaC subunits in cardiac tissue.



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## Hypotheses:

- Rats that are fed a high salt diet will show decreased ENaC expression in the heart
- Rats fed a high salt diet will show decreased cleavage and therefore ENaC activity

## Does salt change ENaC activity in the heart?

## Methods:

- Dahl Salt-Sensitive Male Rats
- Half were given salt water (1% NaCl)
- Other half given normal water



- After 2 weeks their hearts were harvested, homogenized and a Bicinchoninic Acid Assay was performed



- Western blots were performed
- Each blot was probed with :
  - Rabbit Anti-Alpha antibody
  - Rabbit Anti-Beta antibody
  - Rabbit Anti-Gamma antibody

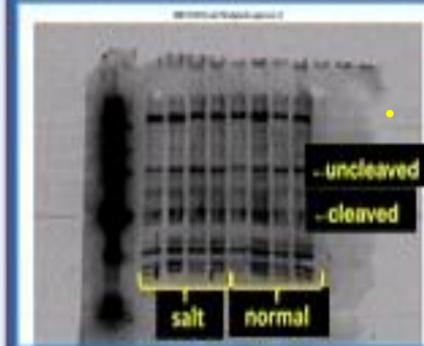
## References:

[1] Awayda M.S., Benigrine A., Hu J.C. and Lis A. "Alternative mechanism of activation of the epithelial Na<sup>+</sup> channel by cleavage." J Biol Chem 284 (2009): 26322-26325 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2794749/?tool=pubmed>

[2] Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Halpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Sotoman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D, Turner MB; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. Circulation. 2012; published online before print December 15, 2011. 10.1161/CIR.0b013e31823ac046

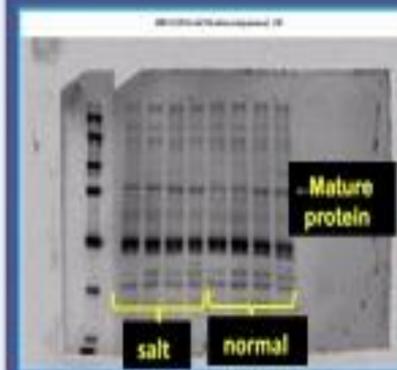
## Results:

### ALPHA SUBUNIT:



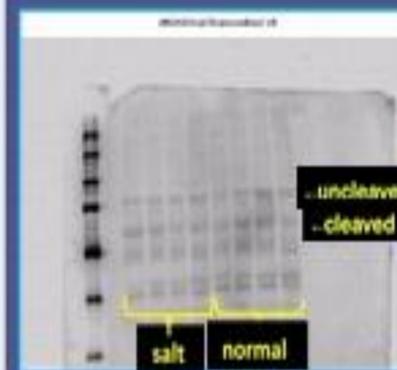
- In high salt rats: the ratio of cleaved to uncleaved is decreased.
- The expression of cleaved subunit is also decreased

### BETA SUBUNIT:



- Full length beta expression was unchanged

### GAMMA SUBUNIT:



- In high salt rats: the ratio of cleaved to uncleaved is decreased.
- The expression of cleaved subunit is also decreased

## Conclusions:

- ENaC in the heart responds to changes of salt intake and likely changes of plasma [Na<sup>+</sup>].
- We propose that ENaC in the heart may serve an integrating function between blood pressure and plasma [Na<sup>+</sup>] whereby if there is too much salt in the diet, ENaC performs negative feedback to prevent salt overload in rats thus, regulating blood pressure.