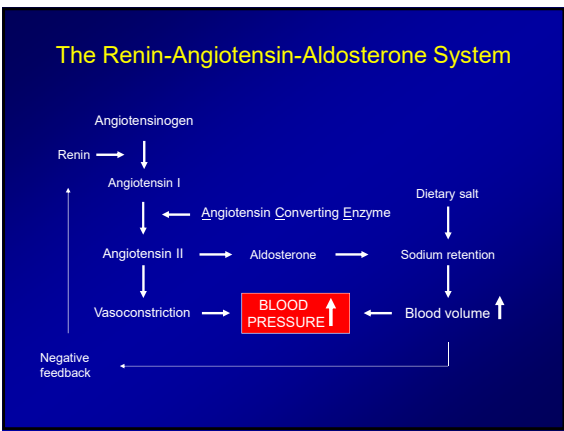
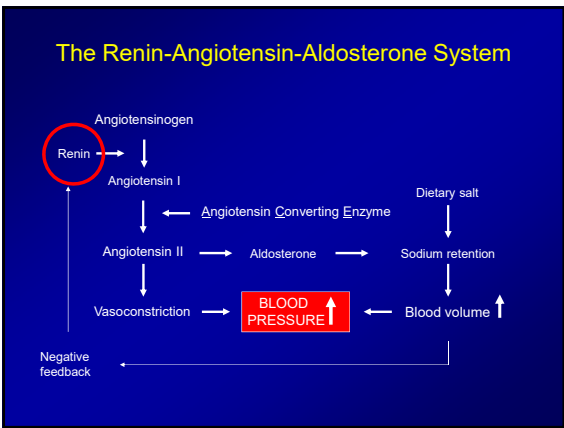


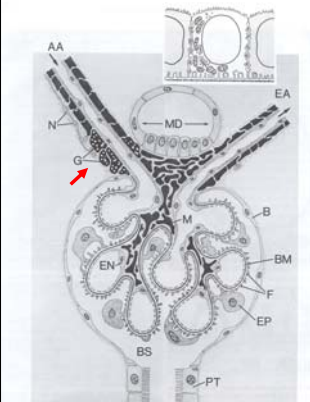
The intrarenal RAS and blood pressure

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Los Angeles, CA

Disclosures: There are NO disclosures or potential conflicts of interest.

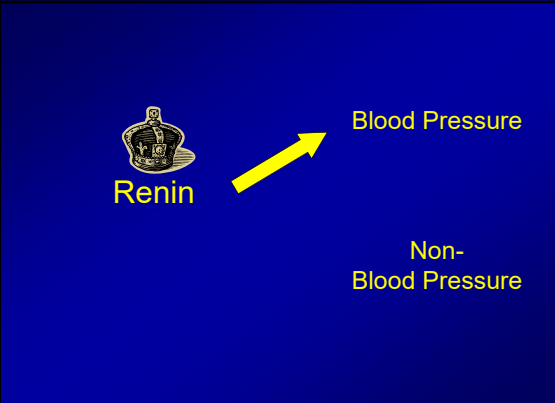






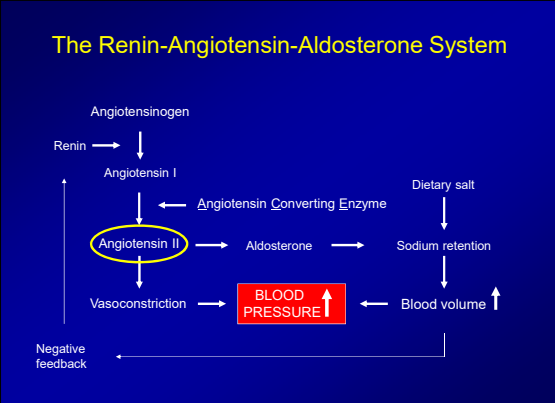
Control of renin secretion:

1. JG cells release active renin
2. cAMP levels critical
 \uparrow cAMP \rightarrow \uparrow Renin
3. Ca^{2+} inhibits renin production
JG cell adenyl cyclase inhibited by increases of Ca^{2+}
 \uparrow Ca^{2+} \rightarrow \downarrow Renin

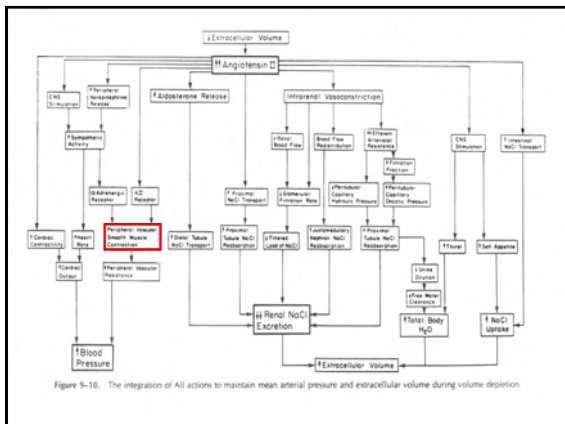


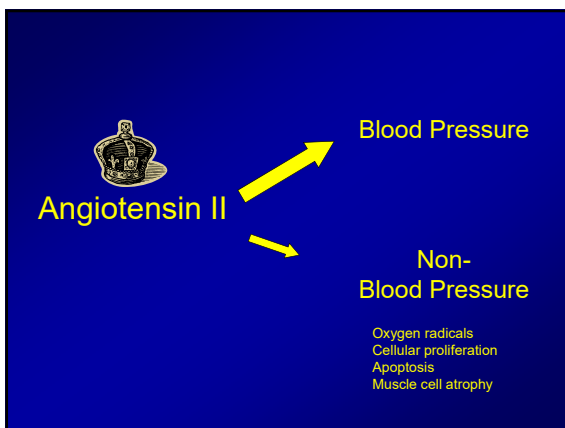
Renin \rightarrow **Blood Pressure**
Non-Blood Pressure

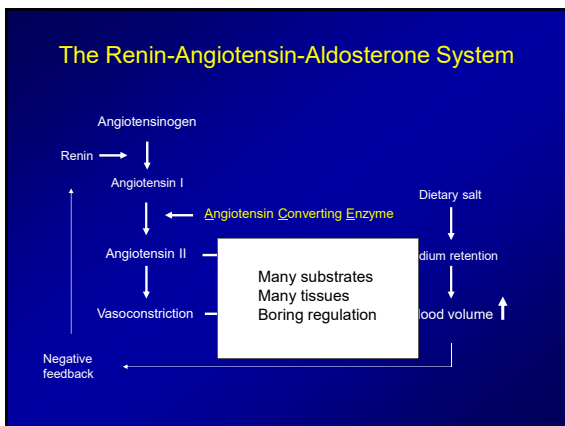
The Renin-Angiotensin-Aldosterone System

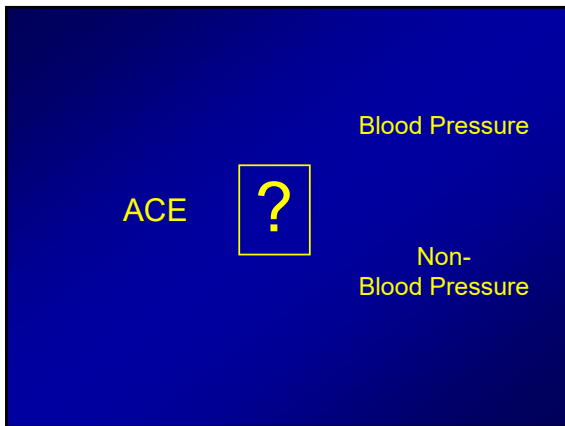


```
graph TD
    Angiotensinogen -- Renin --> Angiotensin_I[Angiotensin I]
    Angiotensin_I -- Angiotensin Converting Enzyme --> Angiotensin_II[Angiotensin II]
    Angiotensin_II --> Vasoconstriction
    Angiotensin_II --> Aldosterone
    Aldosterone --> Sodium_retention[Sodium retention]
    Dietary_salt --> Sodium_retention
    Sodium_retention --> Blood_volume[Blood volume ↑]
    Vasoconstriction --> Blood_pressure[BLOOD PRESSURE ↑]
    Blood_volume --> Blood_pressure
    Blood_pressure -- Negative feedback --> Angiotensinogen
```



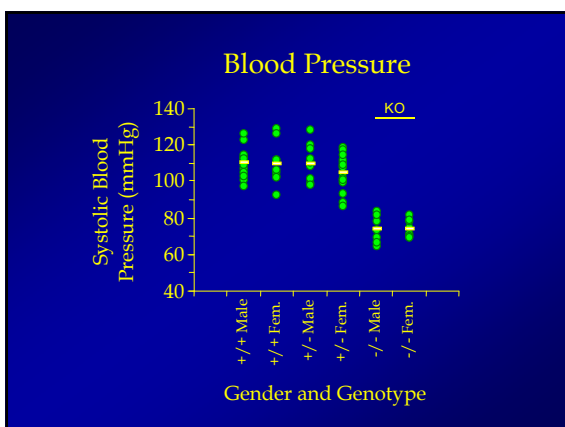






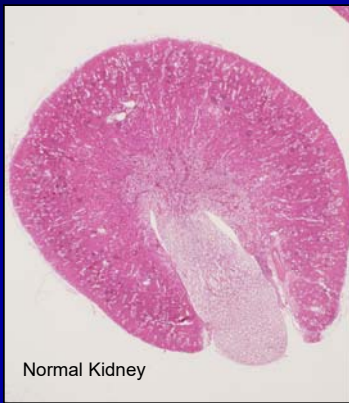
What are the *in vivo* roles of ACE?

1. Blood pressure control



What are the *in vivo* roles of ACE?

1. Blood pressure control
2. Normal urinary flow



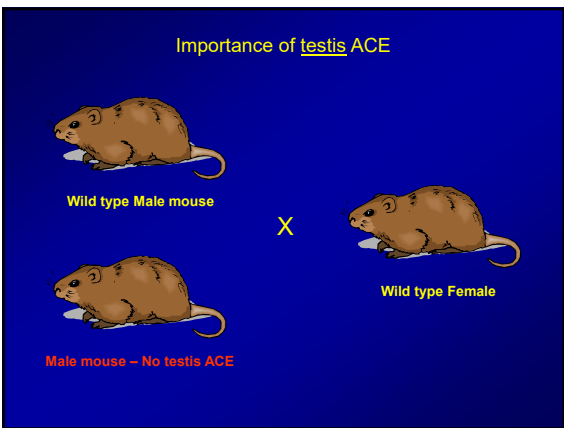
Normal Kidney



ACE.1 KO
Clinical correlates

What are the *in vivo* roles of ACE?

1. Blood pressure control
2. Normal urinary flow
3. Normal male reproduction

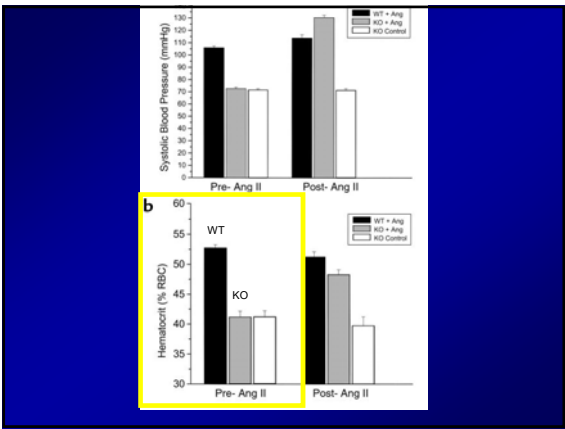


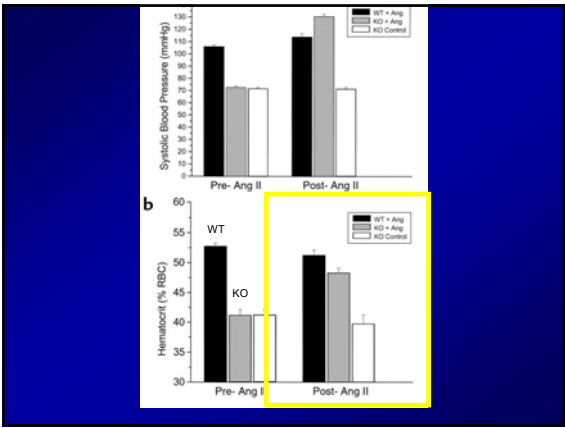
Importance of testis ACE

	Total number of plugs	Total number of litters	Total number of embryos
WT (n=6)	19	15	153
No ACE (n=7)	22	1	1

What are the *in vivo* roles of ACE?

1. Blood pressure control
2. Normal urinary flow
3. Normal male reproduction
4. Normal erythropoiesis





What are the *in vivo* roles of ACE?

1. Blood pressure control
2. Normal urinary flow
3. Normal male reproduction
4. Normal erythropoiesis
5. Normal myelopoiesis

Bone marrow analysis of ACE KO mice

Wright-Giemsa-stained BM cytopsin analysis

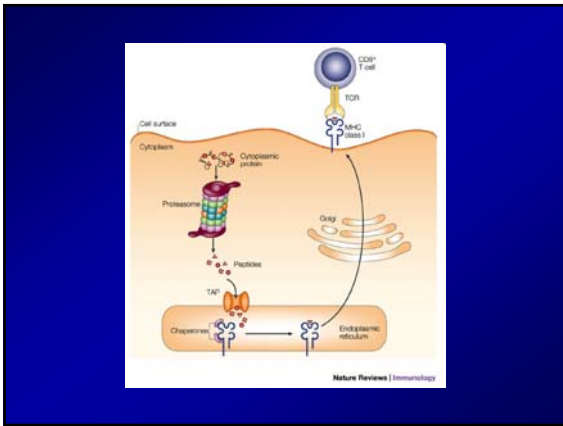
Genotype	Myeloblast	Myelocyte	Meta-myelocyte	Band cell	Segmented cell	Eosinophil	Monocyte/MΦ	Erythroblast
WT	1.7±0.8	3.3±0.3	12.0±2.1	19.8±4.5	23.8±1.2	3.8±0.7	2.4±0.5	2.3±0.3
ACE KO	3.8±0.8	8.3±1.1	17.9±3.8	17.8±3.6	14.9±1.8	8.8±0.4	2.0±0.4	2.3±0.7

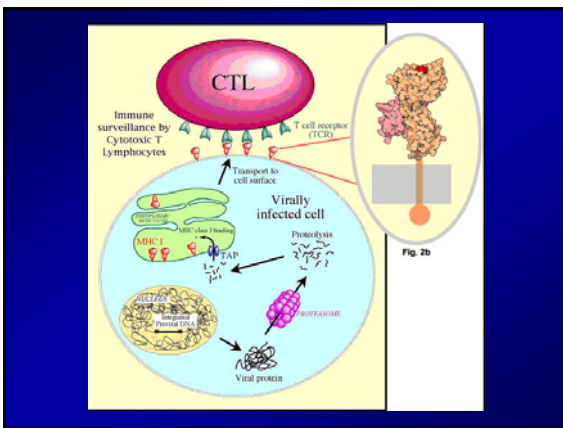
Data are presented as the percentage ± se of total cells and were obtained by counting 400 cells (n=4).

↑ ↑ ↑ ↑

What are the *in vivo* roles of ACE?

1. Blood pressure control
2. Normal urinary flow
3. Normal male reproduction
4. Normal erythropoiesis
5. Normal myelopoiesis
6. MHC class I peptide diversity





Cell, vol. 71, 963-972, December 11, 1992, Copyright © 1992 by Cell Press

Expression of a Membrane Protease Enhances Presentation of Endogenous Antigens to MHC Class I-Restricted T Lymphocytes

Laurence C. Eisenlohr, Igor Bacik, Jack R. Bennink, Kenneth Bernstein, and Jonathan W. Yewdell

Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20906
Department of Pathology, Emory University, Atlanta, Georgia 30322

Expression of Angiotensin-converting Enzyme Changes Major Histocompatibility Complex Class I Peptide Presentation by Modifying C Termini of Peptide Precursors

Xiao Z. Shen, Aron E. Lukacher, Sandrine Billet, Ifor R. Williams, and Kenneth E. Bernstein

From the Department of Pathology, Emory University School of Medicine, Atlanta, Georgia 30322

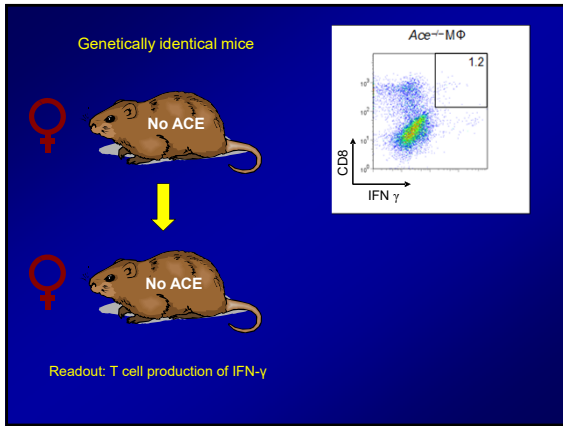
JBC, April, 2008.

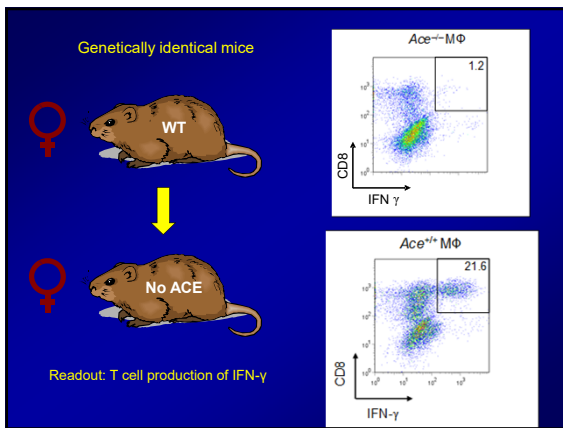
Genetically identical mice

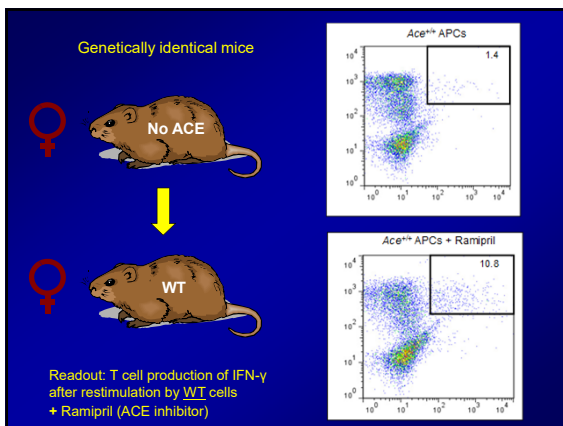
Readout: T cell production of IFN- γ

Genetically identical mice

Readout: T cell production of IFN- γ







Conclusion: Under 'normal' physiologic conditions, the carboxypeptidase ACE plays a role in shaping the MHC class I peptide repertoire!!!

...at least in mice

