Prevalence of Hypertension in U.S. Men by Age and Ethnicity

Adapted from Burt et al. Hypertension 1995;25:305.
Hypertension is often called the “silent killer” because many people who are hypertensive don’t know it. Over time, if untreated, high blood pressure can lead to stroke, heart attack, heart failure, kidney and vascular disease.
The Renin-Angiotensin System (RAS)

- angiotensinogen → renin
  - angiotensin I → angiotensin II
  - AT2 Receptors: vasodilation, Na Excretion
  - AT1 Receptors: vasoconstriction, Na Retention

- Drugs used to block RAS:
  - renin inhibitor
  - angiotensin converting enzyme inhibitors
  - AT1 receptor antagonists

- BP & organ protection
- BP & end organ damage
Role of the Kidney in Blood Pressure Regulation

ECF Volume → Blood Volume → Stroke Volume
Humoral → TPR

\[ X \times \text{CO} = \text{Blood Pressure} \]
The renal nephron

- afferent arteriole
- macula densa
- juxtaglomerular cells (renin release)
- thick ascending limb
William Beierwaltes: Calcium regulation of renin release
Mariela Mendez: Molecular mechanisms of renin release

renin

ROS

VAMP 2

SNAP23

syntaxin

renin
The renal nephron

thick ascending limb →
Jeffrey Garvin: Regulation of thick ascending limb transport by NO and $O_2^-$

![Diagram showing the regulation of transport by NO and $O_2^-$]
Pablo Ortiz: Trafficking of the Na/K/2 Cl cotransporter and changes caused by hypertension

Diagram:
- **dynamin2**
- **Endocytosis**
- **NKCC2**
- **Recycling pool**
- **VAMP 2**
- **cAMP**
- **TAL epithelium**
- **Apical membrane**

**AVP**
O. Carretero and J. Garvin: Regulation of the renal microvasculature by nephron NaCl absorption

- connecting tubule
- afferent arteriole
- macula densa
Connecting tubule glomerular feedback

Afferent arteriolar diameter (um)

[Graph showing the relationship between CNT NaCl concentration in mM and afferent arteriolar diameter (um).]

- CNT NaCl concentrations: 10, 20, 40, 80 mM
- Afferent arteriolar diameter decreases from 20 um at 10 mM to 14 um at 80 mM

Af-Art and CNT, L-NaCl
End Organ Damage
Oscar Carretero: Ac-SDKP reduces inflammation and end organ damage caused by hypertension

Hypertension

Thymosin β4

Ac-SDKP

Inflammation

Cardiac and renal fibrosis/dysfunction
Nour-Eddine Rhaleb: Mechanism by which Ac-SDKP prevents end organ damage and identifying its receptor

Ac-SDKP → Receptor → Hypertension → Inflammation → Fibrosis → Dysfunction

**Rat myocardium**

<table>
<thead>
<tr>
<th>Ac-SDKP (µM)</th>
<th>0</th>
<th>10</th>
<th>100</th>
<th>1000</th>
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<td>125I-Hpp-Aca-SDKP (1 µM)</td>
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- Ac-SDKP (µM) → 75 kDa
- Ac-SDKP (µM) → 50 kDa

- CTL
- ALDO-salt + Vehicle
- ALDO-salt + ACEi
- ALDO-salt + Ac-SDKP
- ALDO-salt + Ac-SDKP + mAb
- ALDO-salt + ACEi + mAb
Suresh Palaniyandi: Role of aldehyde dehydrogenase in protecting the heart from damage

- Diabetes $\rightarrow$ Hyperglycemia $\rightarrow$ ROS
- ROS $\rightarrow$ Toxic aldehydes accumulation & ALDH activity
- ALDH activator

End Organ Damage
Xiao-Ping Yang: Role of AT2 receptors in cardiac organ damage

Angiotensin II

$\text{AT}_1\text{R}$

Vasoconstriction
Aldosterone
Sympathetic activity
Fibrosis, growth
ROS
Inflammation
Apoptosis

$\text{AT}_2\text{R}$

PRCP
ACE2
Kinins, Ang-(1-7), NO

Vasodilatation
Anti-fibrotic; anti-growth
Anti-inflammation
Anti-apoptosis

EOD
Pamela Harding: Role of the EP4 receptor in protecting the heart

**Graphs and Images:**

- **Bar Graphs:**
  - Top left: EF (%) bar graph with sham and MI groups, showing a significant difference (P < 0.05) with n = 8-14.
  - Bottom left: LVDs (mm) bar graph with sham and MI groups, showing a significant difference (P < 0.05) with n = 8-14.

- **Histology Images:**
  - WT
  - EP4 KO

- **Line Graph:**
  - Graph showing PS/L (%) over time (ms) with 1 Hz pacing, demonstrating different responses across WT, KO-H, and KO-L.

**Legends:**
- WT
- KO-H
- KO-L

**Additional Notes:**

- EF (%): EF is measured in percentage.
- LVDs (mm): LVDs are measured in millimeters.
- PS/L (%): PS/L is measured in percentage.
- Time (ms): Time is measured in milliseconds.
- 1 Hz Pacing: Indicates the pacing frequency.
Edward Shesely, Ph.D.
Director Mutant Mouse Core

Current strains
AT2 -/y
B1 -/
B2 -/
CCCR2 -/
Galectin 3 -/
nNOS -/
e,nNOS -/
PGE synthase 1 -/
EP4 - cardiac specific
VAMP 3 -/
VAMP 8 -/
NFκβ luciferase
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<td>J.L. Garvin</td>
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<td>Blood pressure regulation: Novel roles of the kidney</td>
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