News in sodium balance

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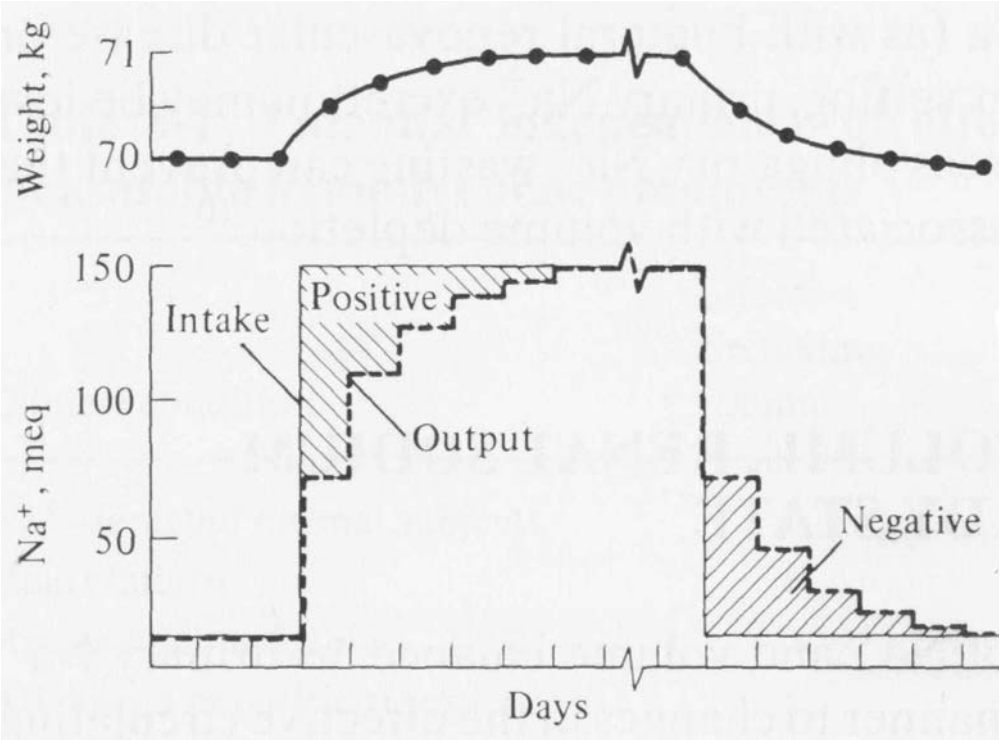
Universitätsklinikum Erlangen

Sodium balance in humans:

What goes in, must come out…



Maxwell & Kleeman: Clinical Disorders of Fluid and Electrolyte Metabolism, McGraw Hill, 1972

News in sodium balance

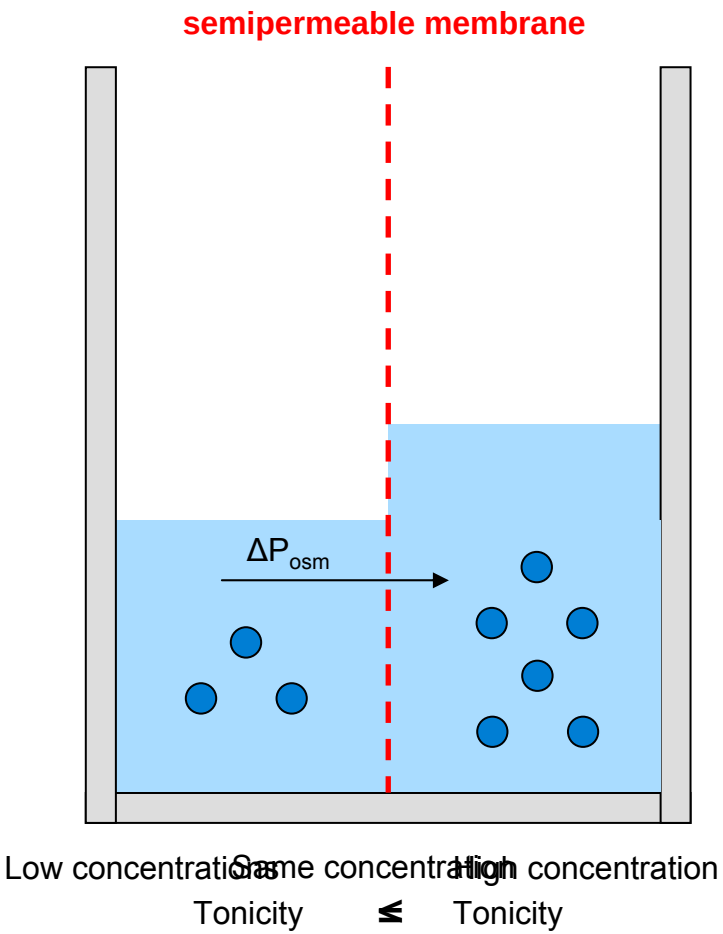
I. Underlying concept: isotonicity of body fluids.

II. A look inside the body: water-free Na^+ retention.

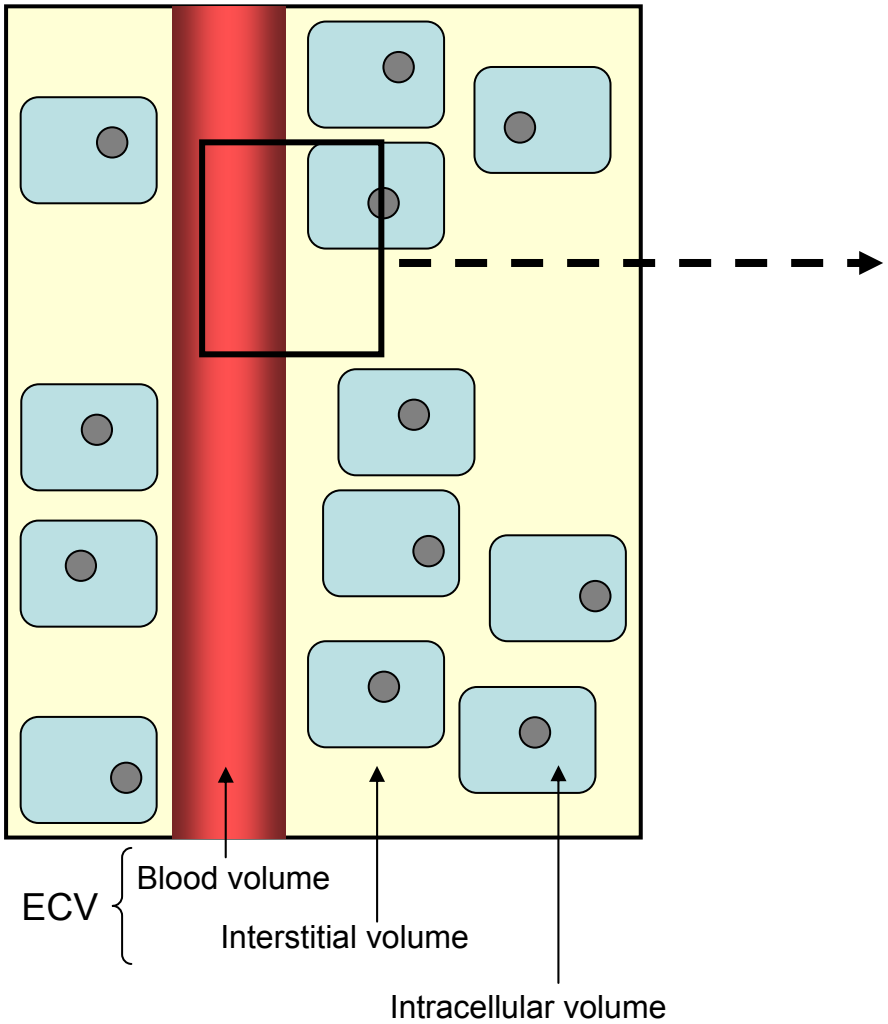
III. Interstitial sodium control: cells of the monocyte phagocyte system (MPS) as regulators of volume and blood pressure homeostasis

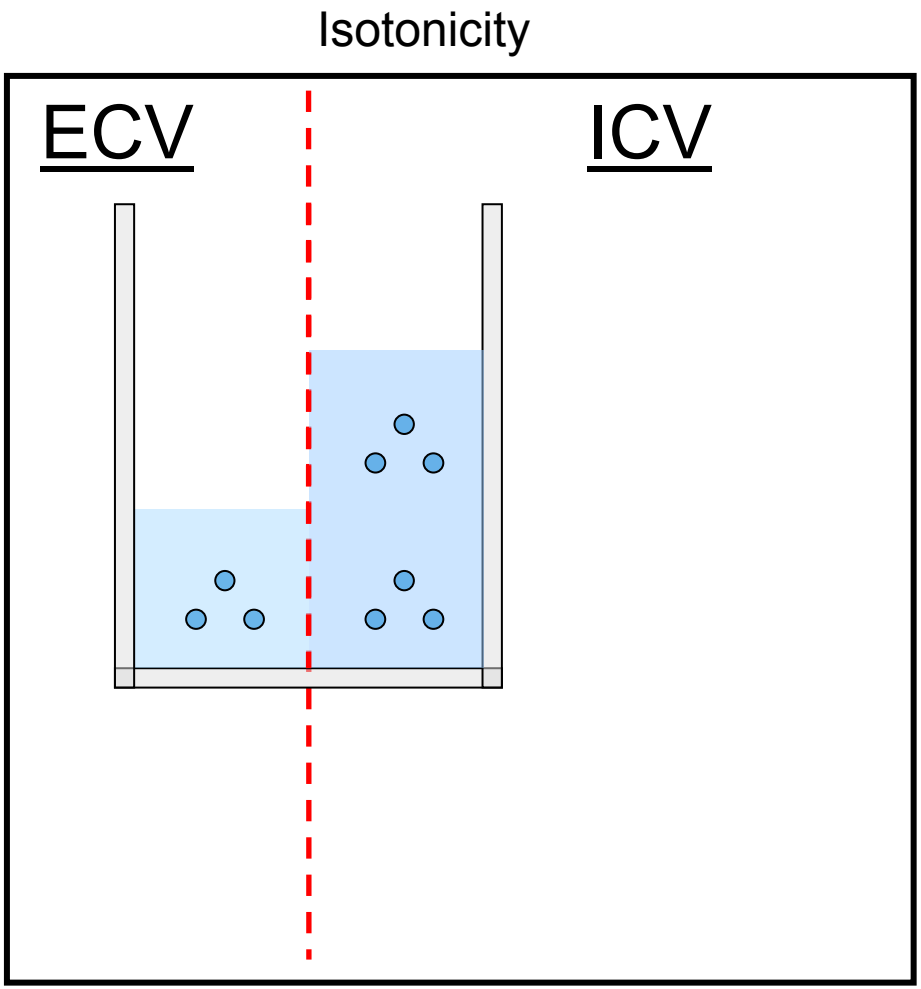
a. MPS cells and osmotic stress.
b. MPS cells and lymphatic capillaries.
c. MPS cells and blood pressure regulation.

Tonicity of body fluids



Tonicity and the internal environment





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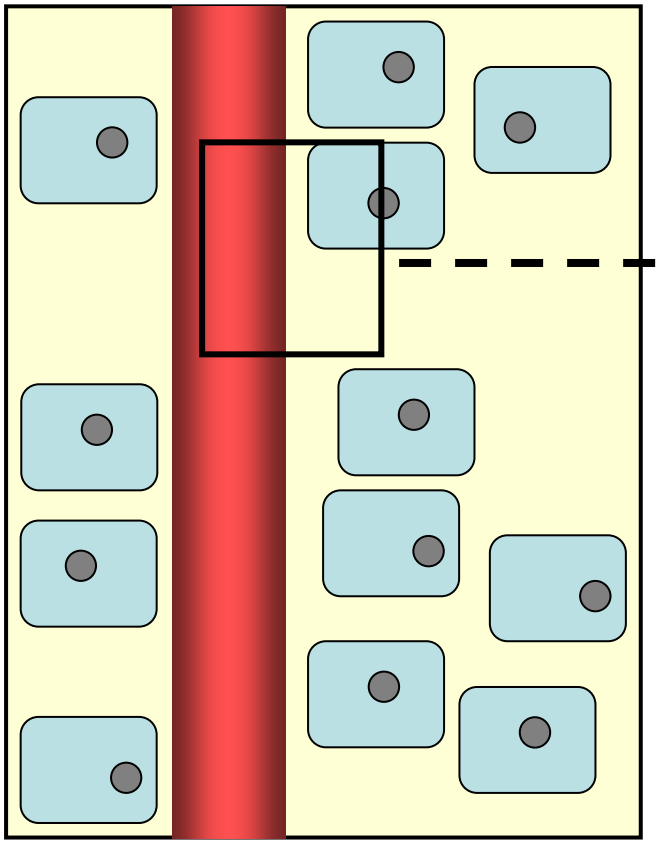
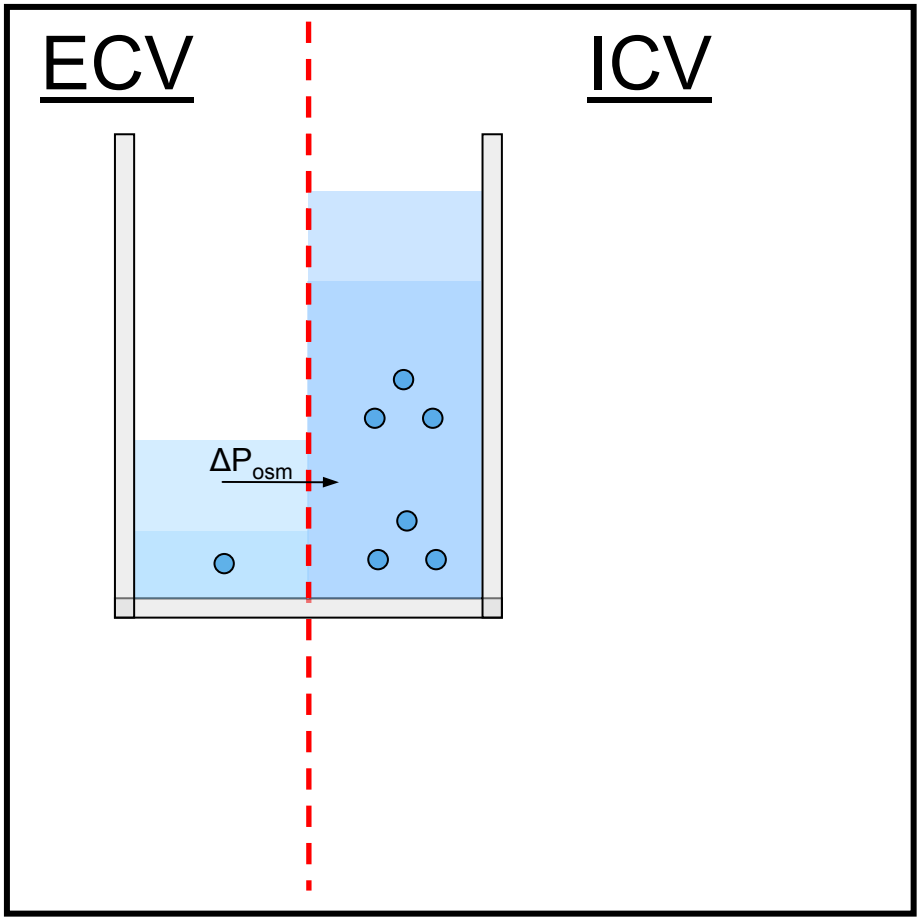


Extracellular hypotonicity



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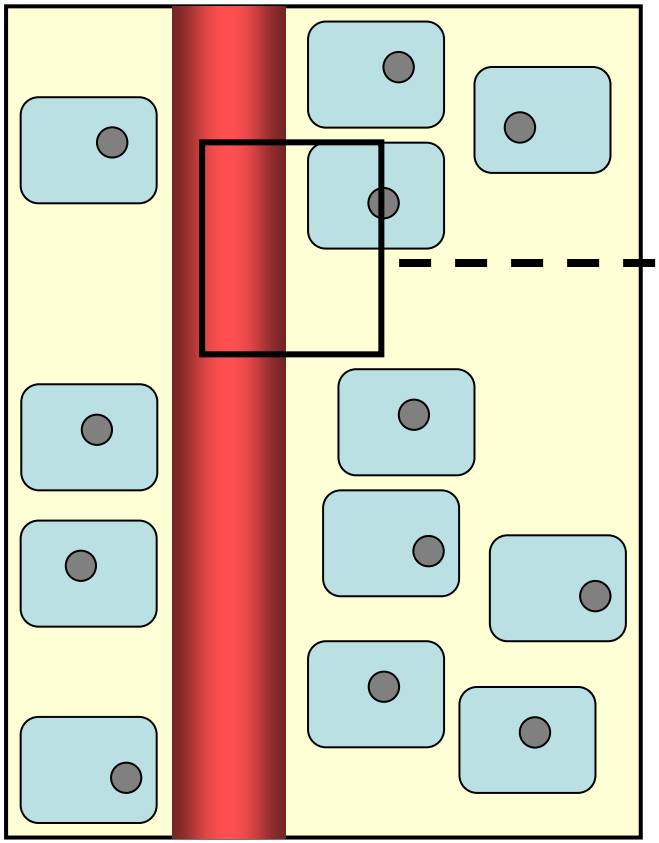
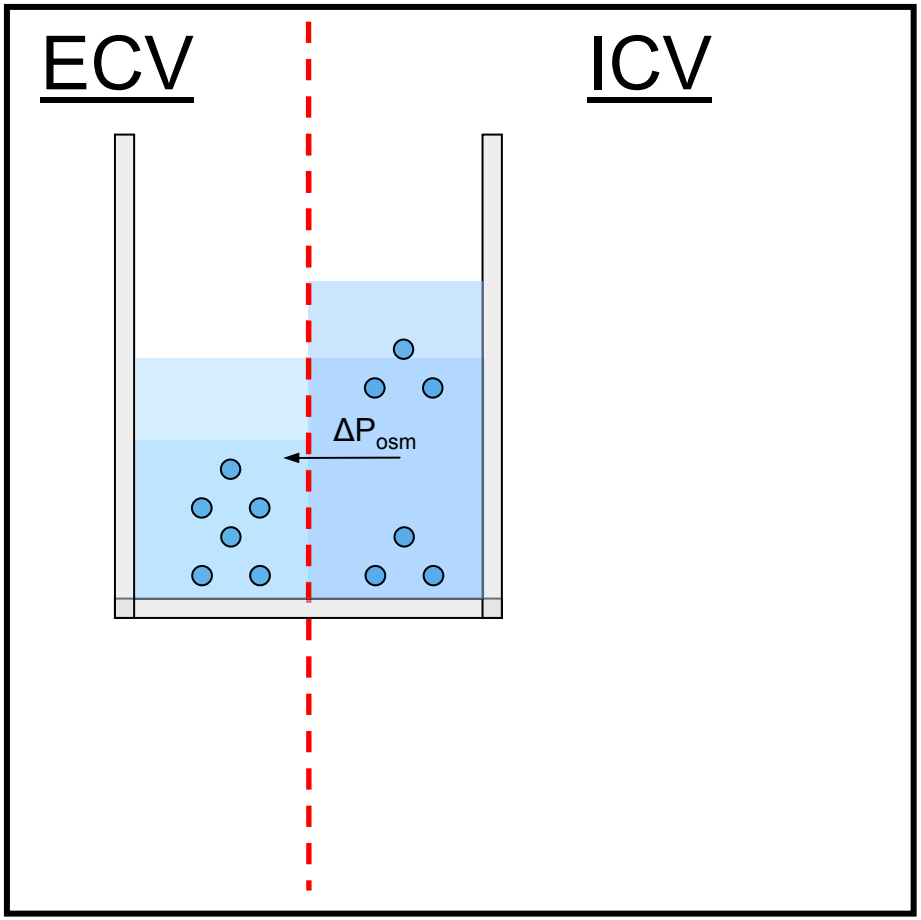


Extracellular hypertonicity



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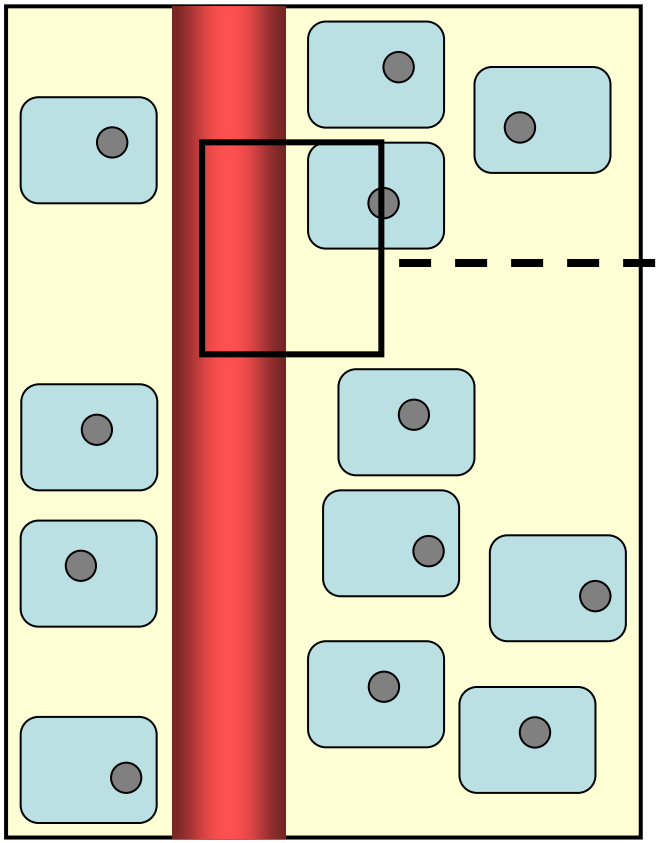
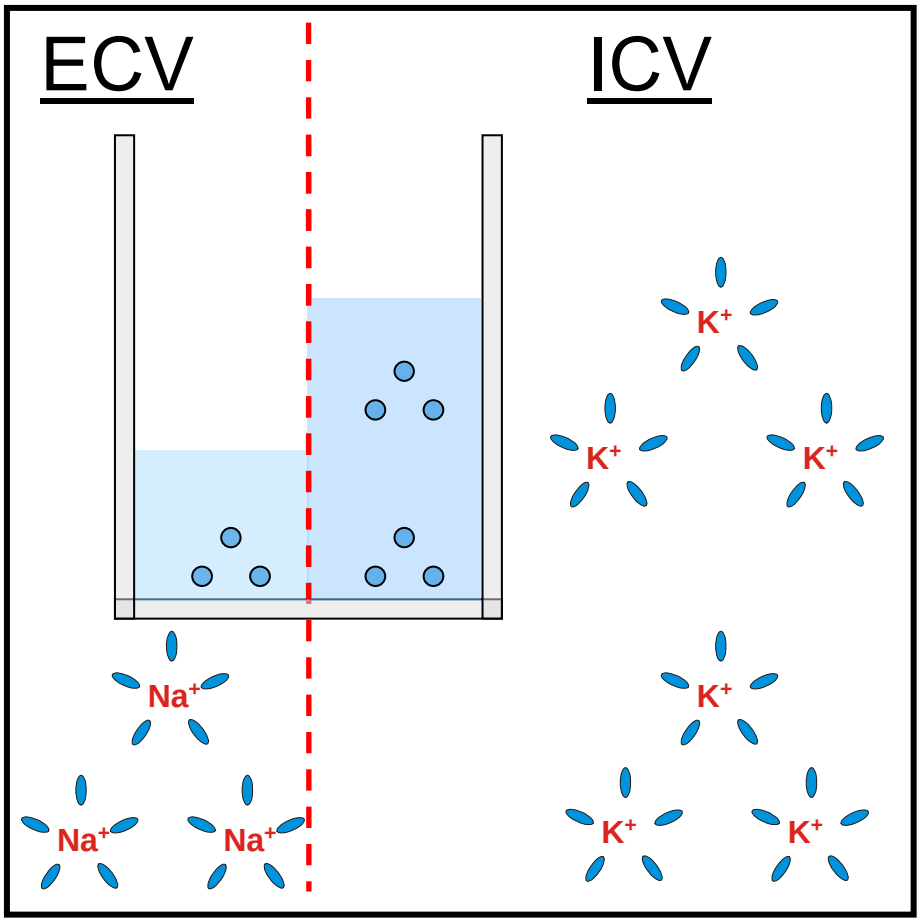


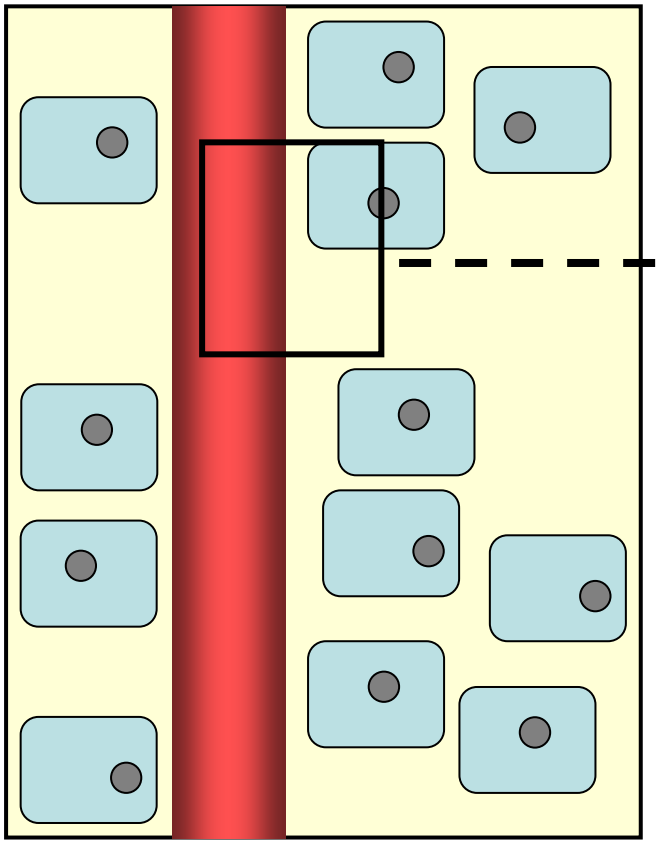


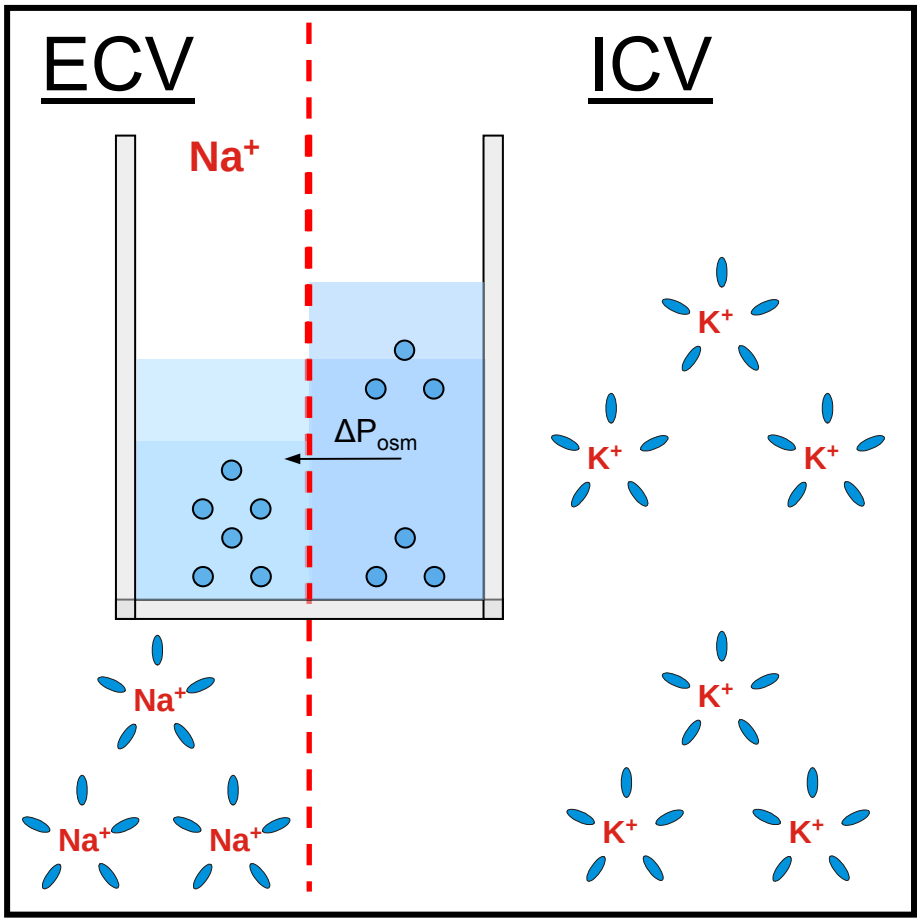
Isotonicity:

≈ 140 mmol/L

≈ 140 mmol/L

Tonicity and the internal environment





Isotonicity:

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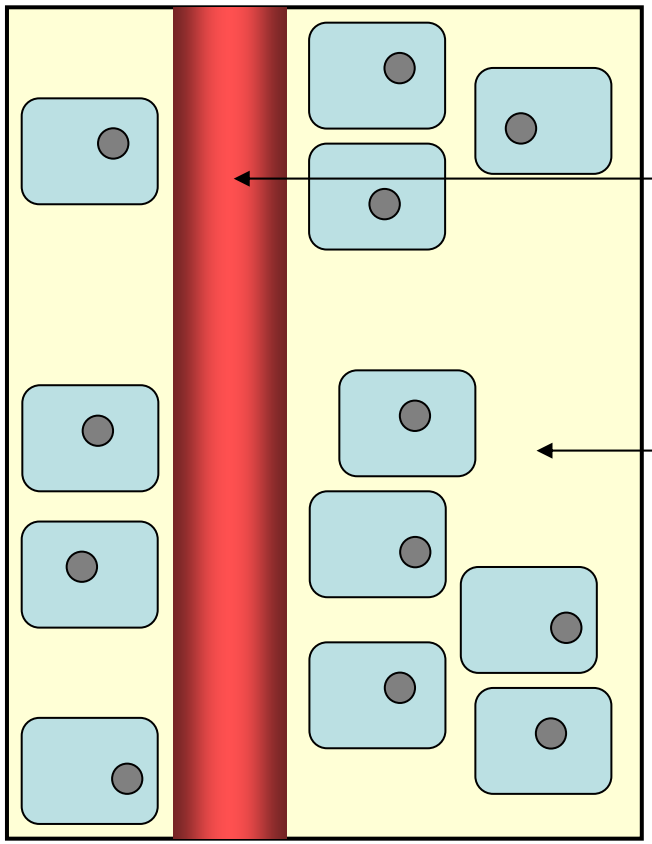
A look inside the body: water-free Na^+-retention

Haljamäe H, Linde A, Amundson B.
Am J Physiol 227 (1974) 1199-1205

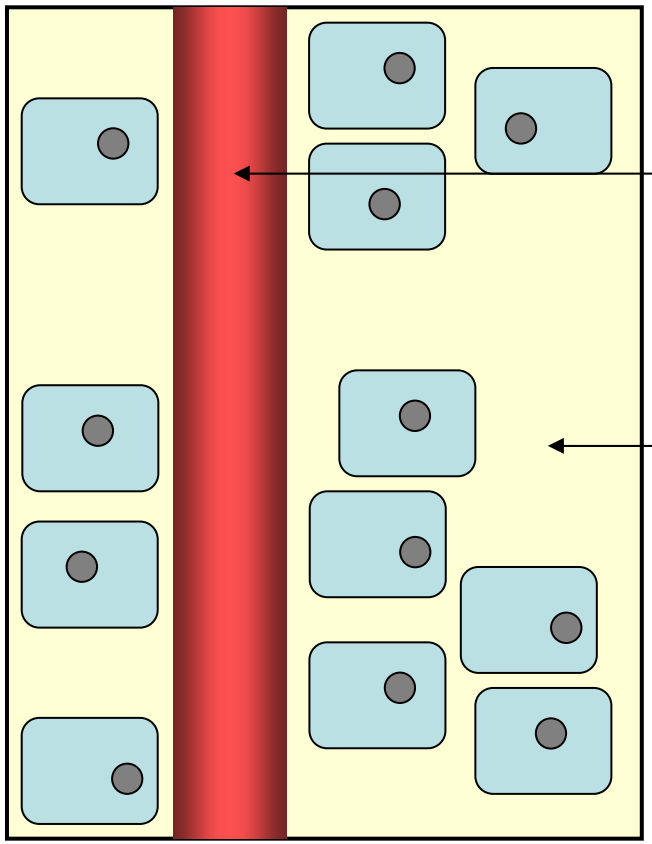


Blood: $[Na^+]$ = 146.9 mmol/L

Interstitium: $[Na^+]$ = 156.2 mmol/L

A look inside the body: water-free Na^+-retention

Szabo G, Magyar Z.
Lymphology 15 (1982) 174-177

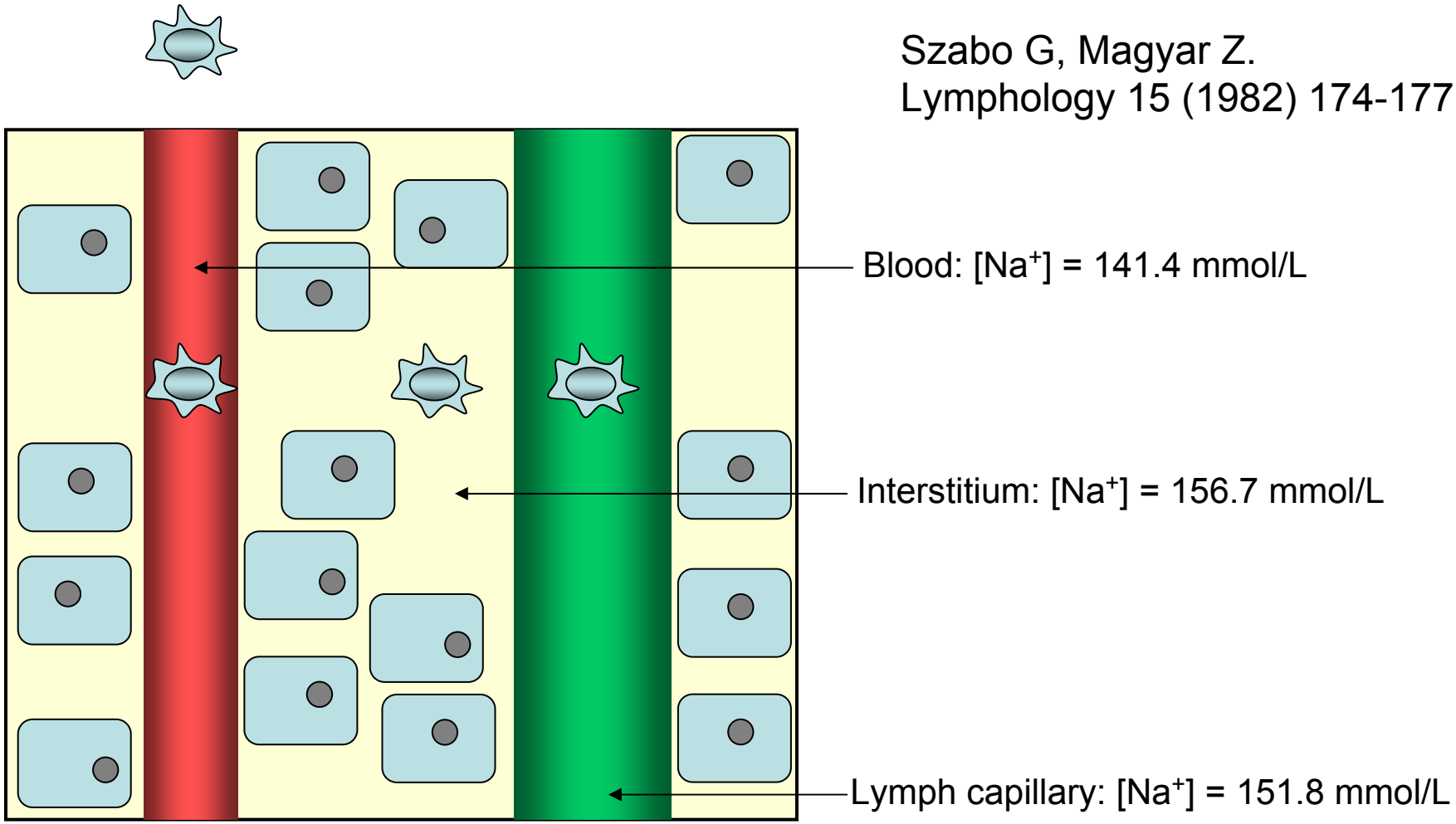


Blood: $[Na^+]$ = 141.4 mmol/L

Interstitium: $[Na^+]$ = 156.7 mmol/L

A look inside the body: water-free Na^+-retention

Szabo G, Magyar Z.
Lymphology 15 (1982) 174-177



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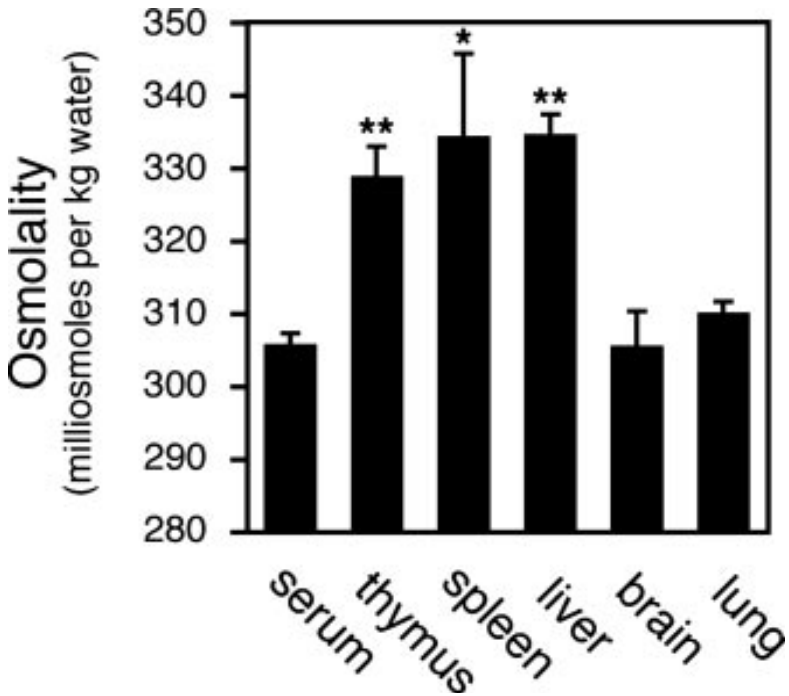
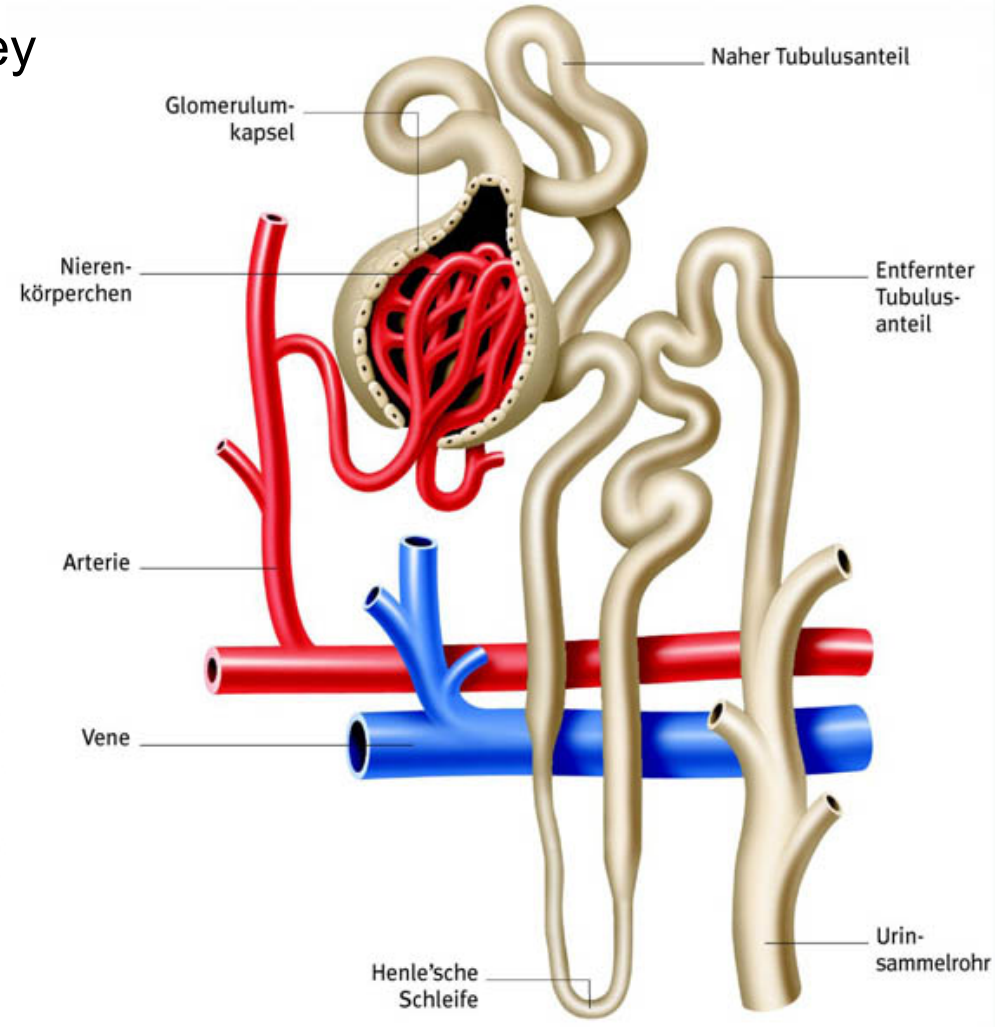


Go, W.Y. et al.:
PNAS 101 (29):10673-10678, 2004.

A look inside the body: water-free Na^+ retention

Analogy to the kidney



300 mOsm / kg

400 mOsm / kg

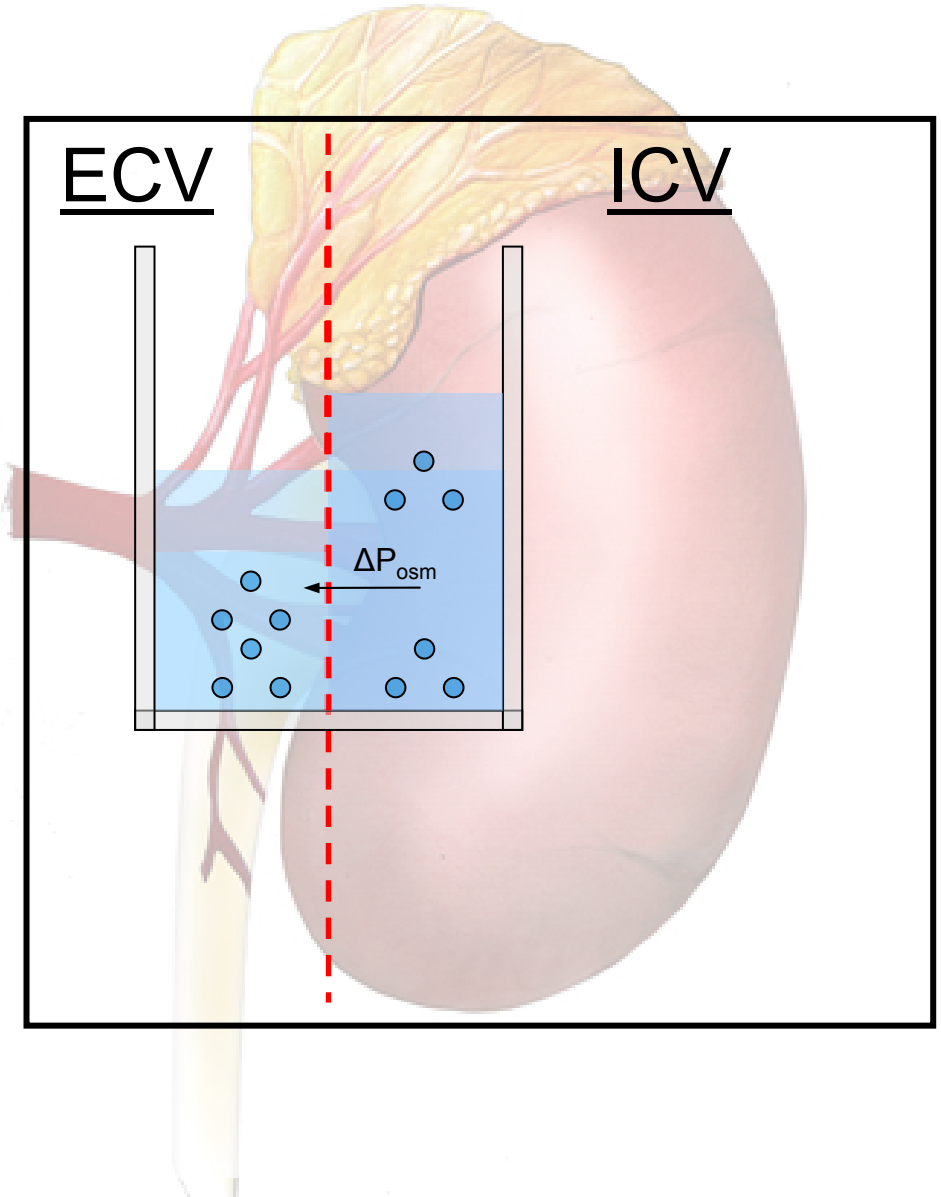
600 mOsm / kg

800 mOsm / kg

1000 mOsm / kg

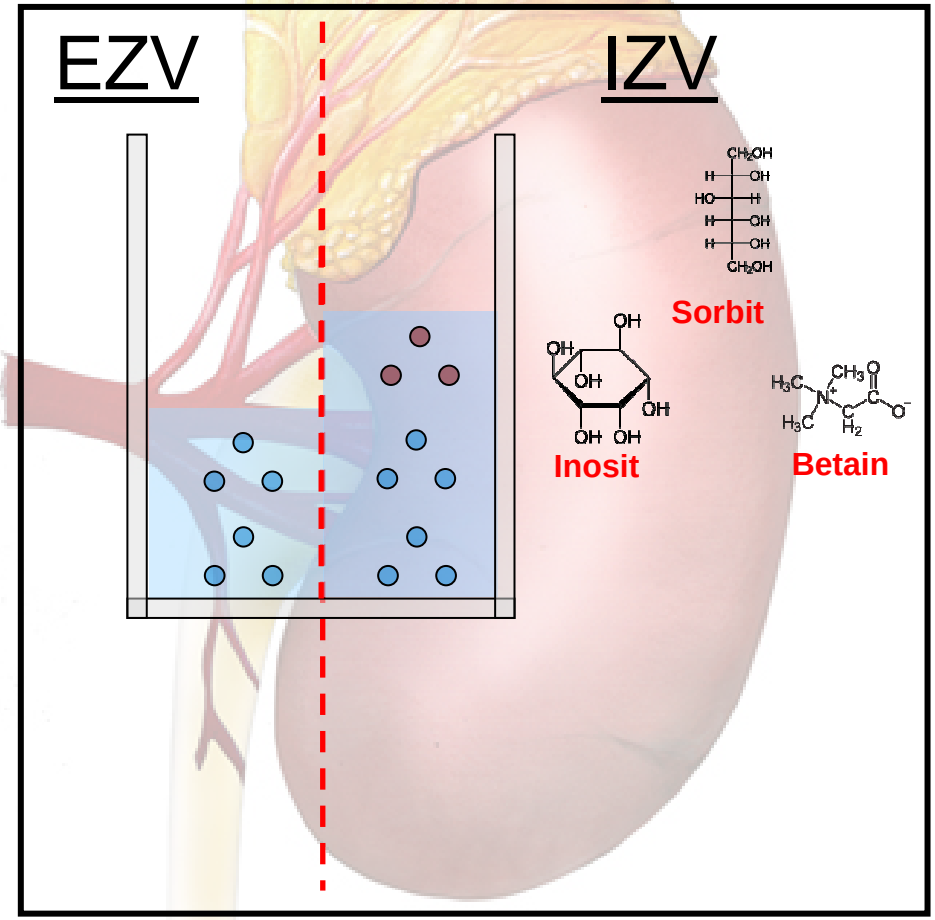
1200 mOsm / kg

A look inside the body: water-free Na^+ retention in the kidney

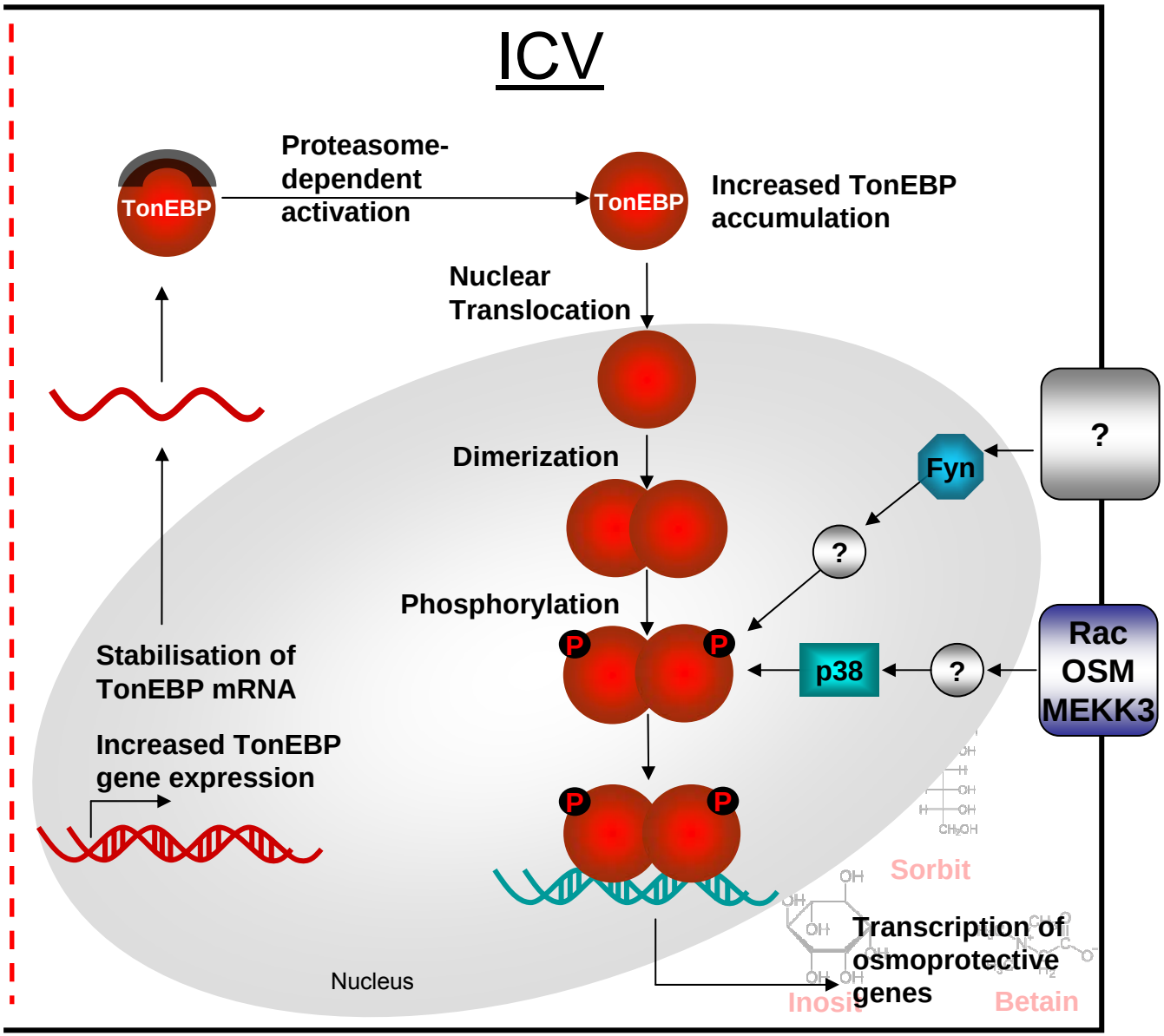


A look inside the body: water-free Na^+ retention

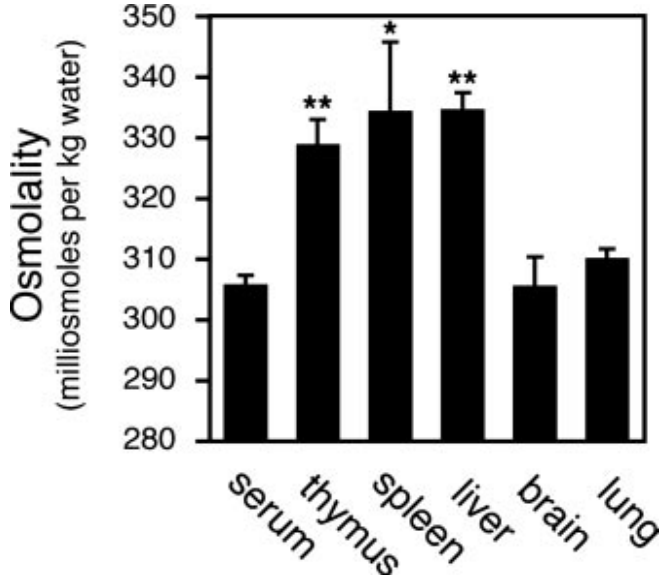
How the kidney protects itself from osmotic stress

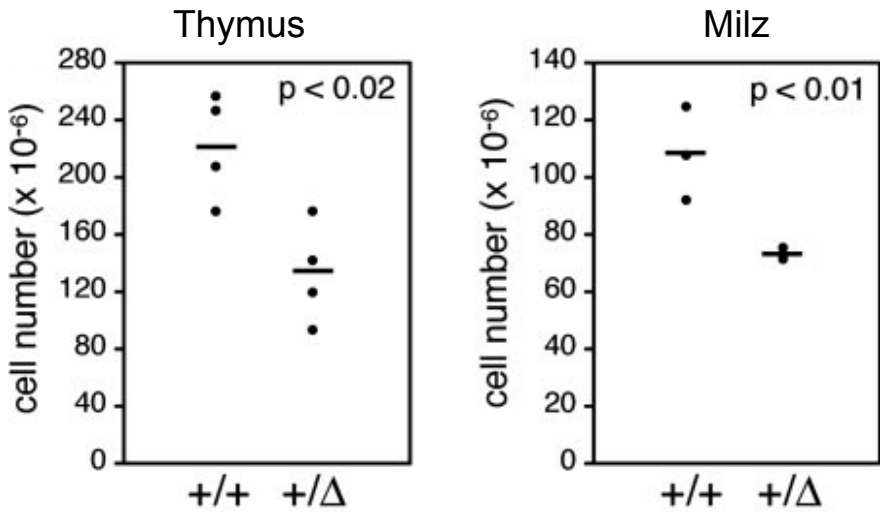


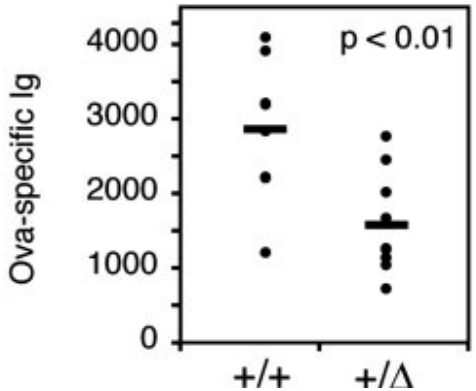
A look inside the body: water-free Na^+ retention



A look inside the body: water-free Na^+-storage







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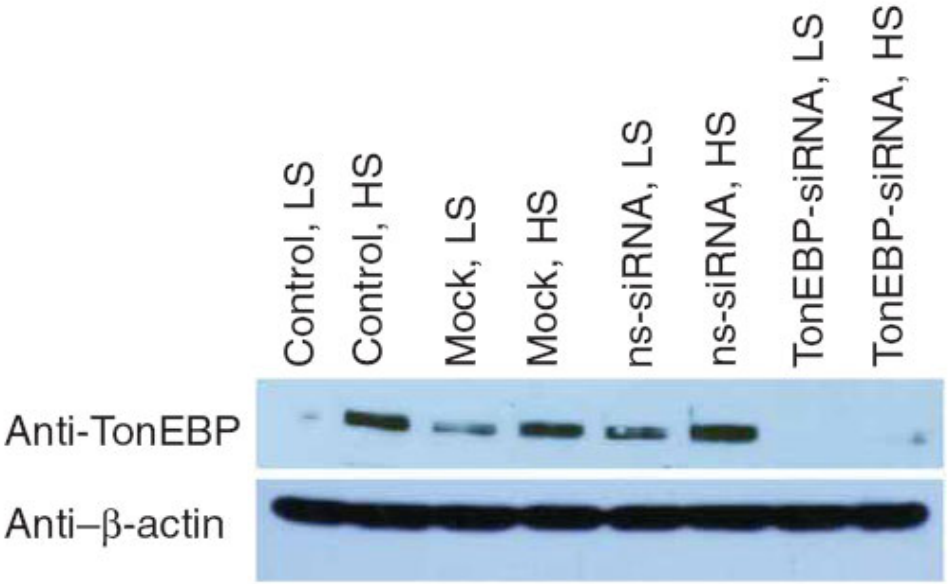
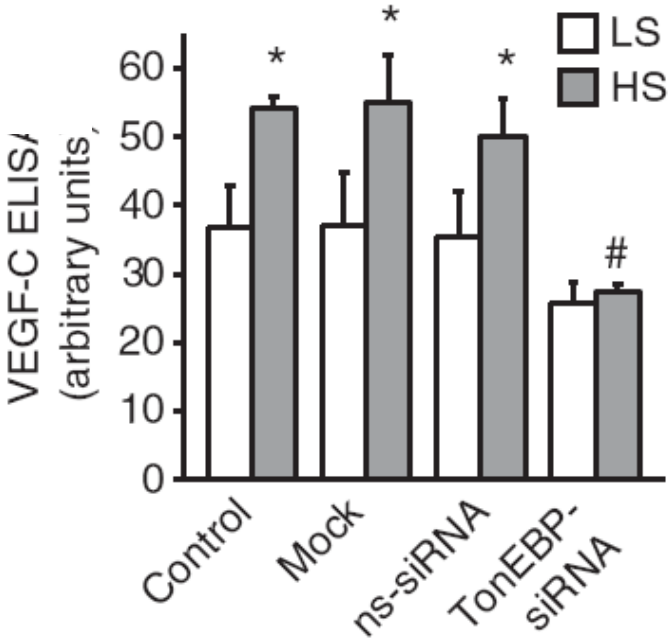
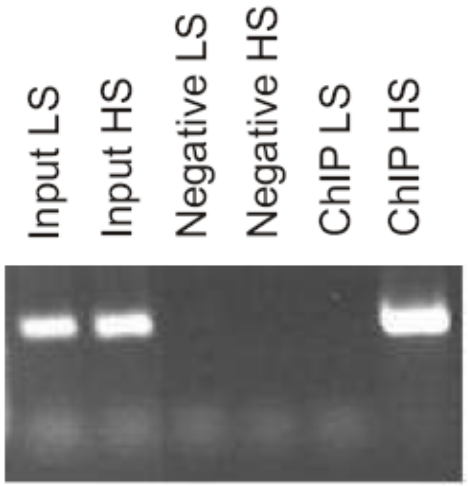
Macrophages as “interstitial sensors”, and VEGF-C as an “osmoprotective gene”



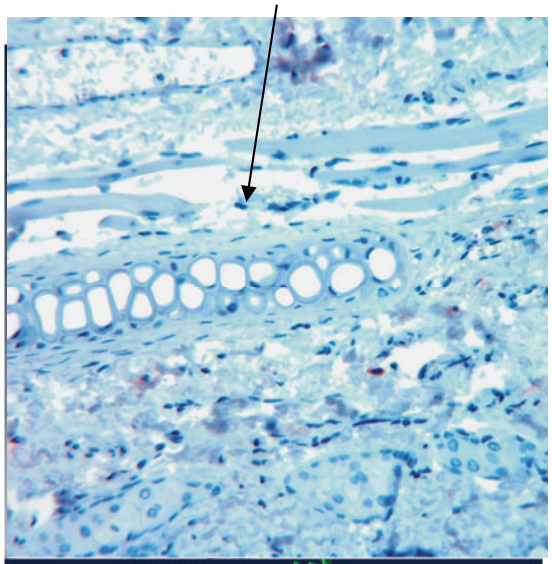


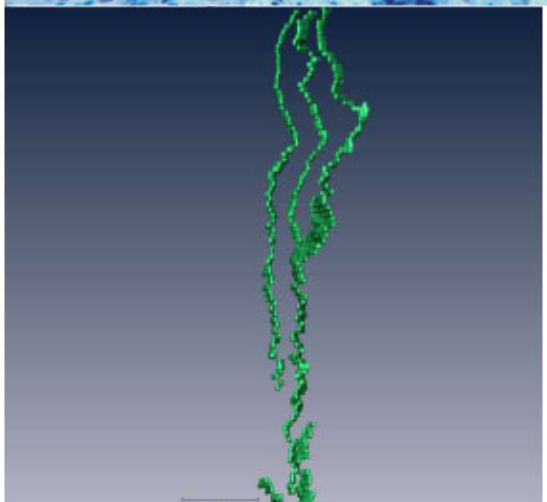


Nat Med 15 (5): 545-552, 2009

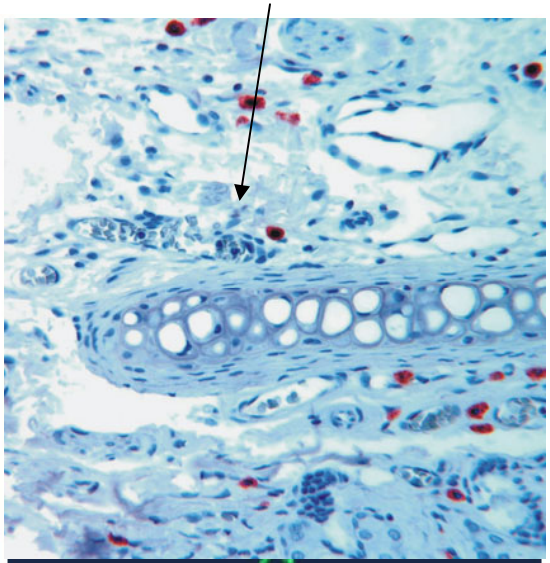
Macrophages as regulators of volume and blood pressure homeostasis

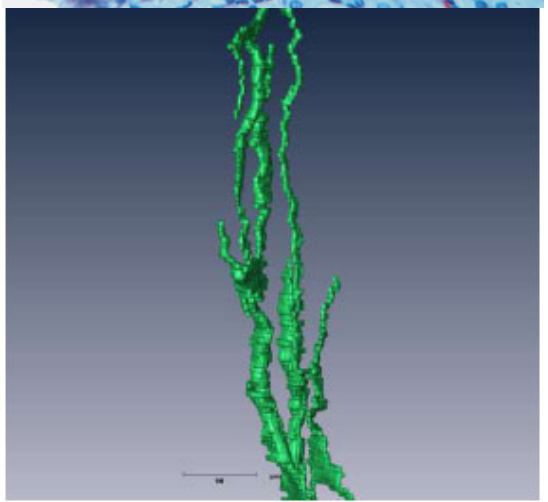
$(Na^+ + K^+)/H_2O \approx 160 - 170$ mmol/L





$(Na^+ + K^+)/H_2O \approx 180 - 200$ mmol/L





Na^+-induced hypertonicity

TonEBP Binding Sit

TonEBP activation

Nat Med 15 5): 545-552, 2009

MPS cells and lymphatics

	LSD	HSD
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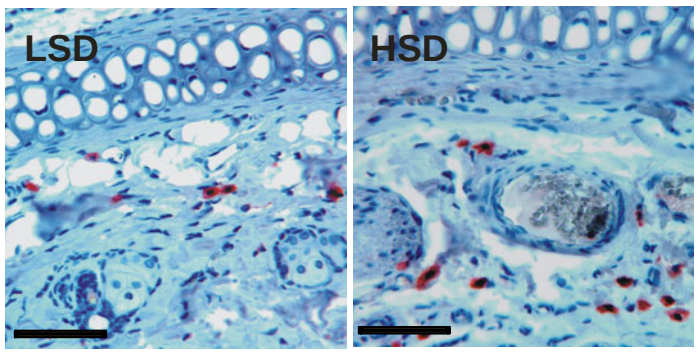
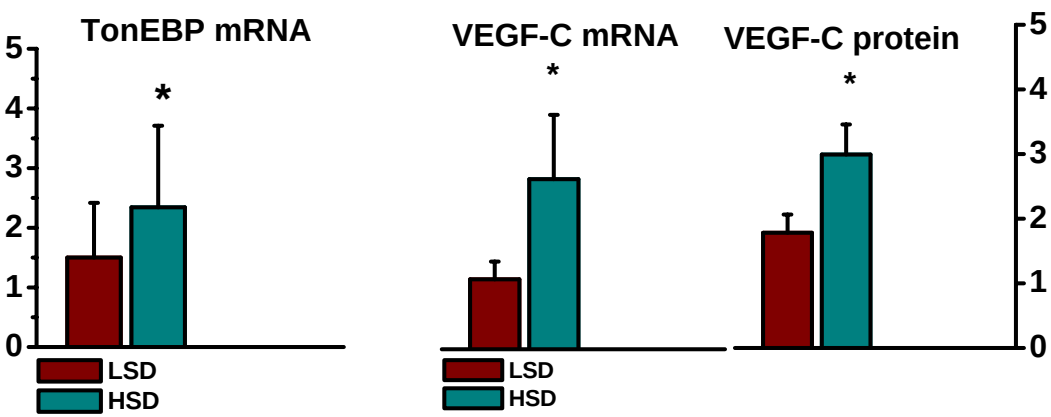
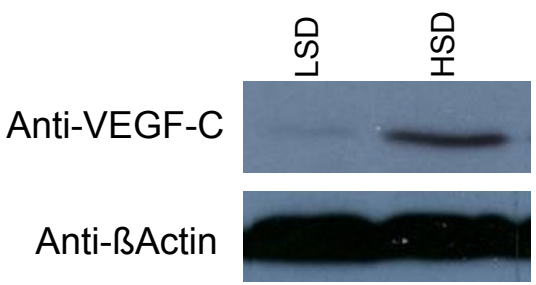


Is MPS cell infiltration paralleled by increased VEGF-C expression?





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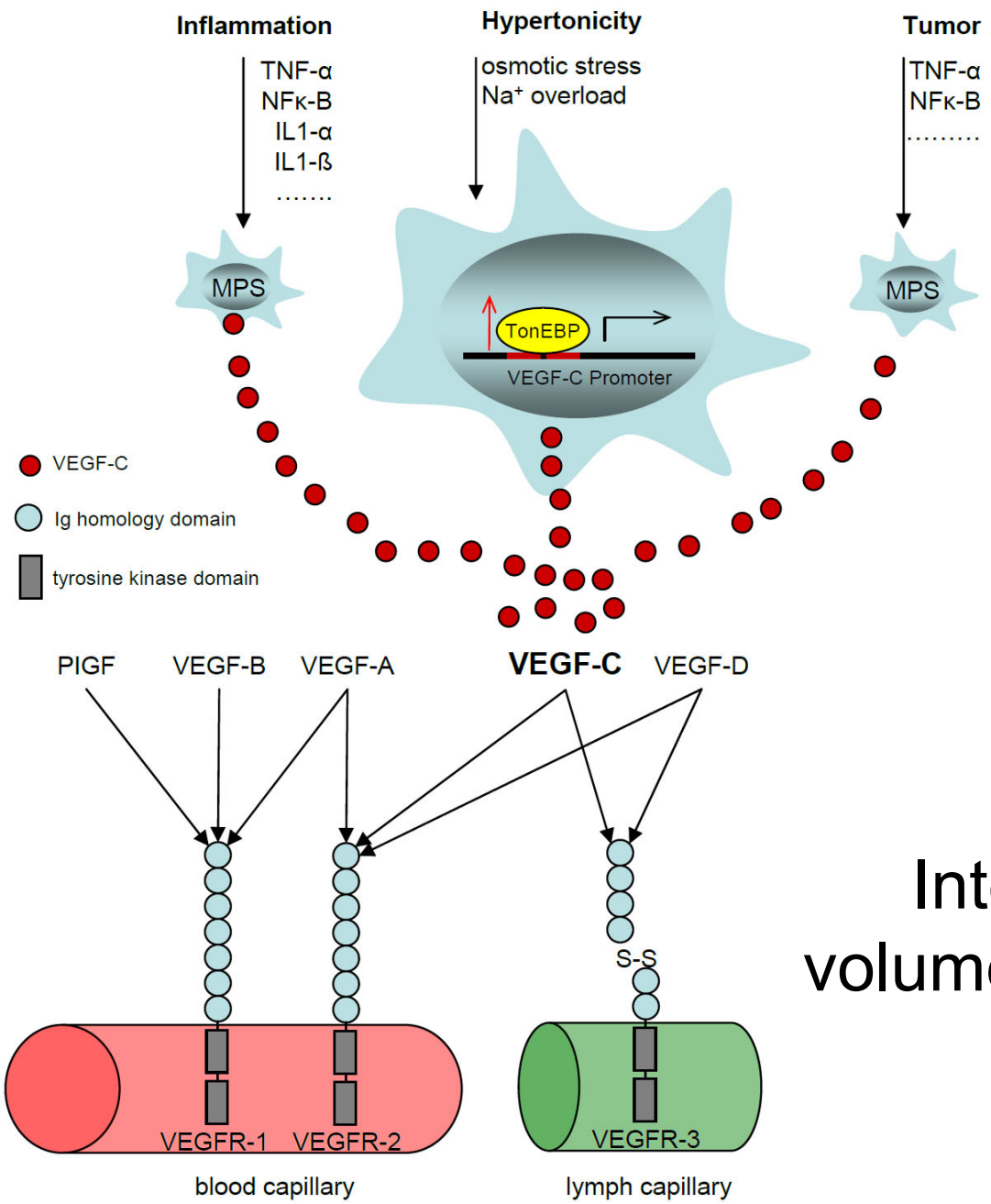

eNOS

Interstitial volume transport

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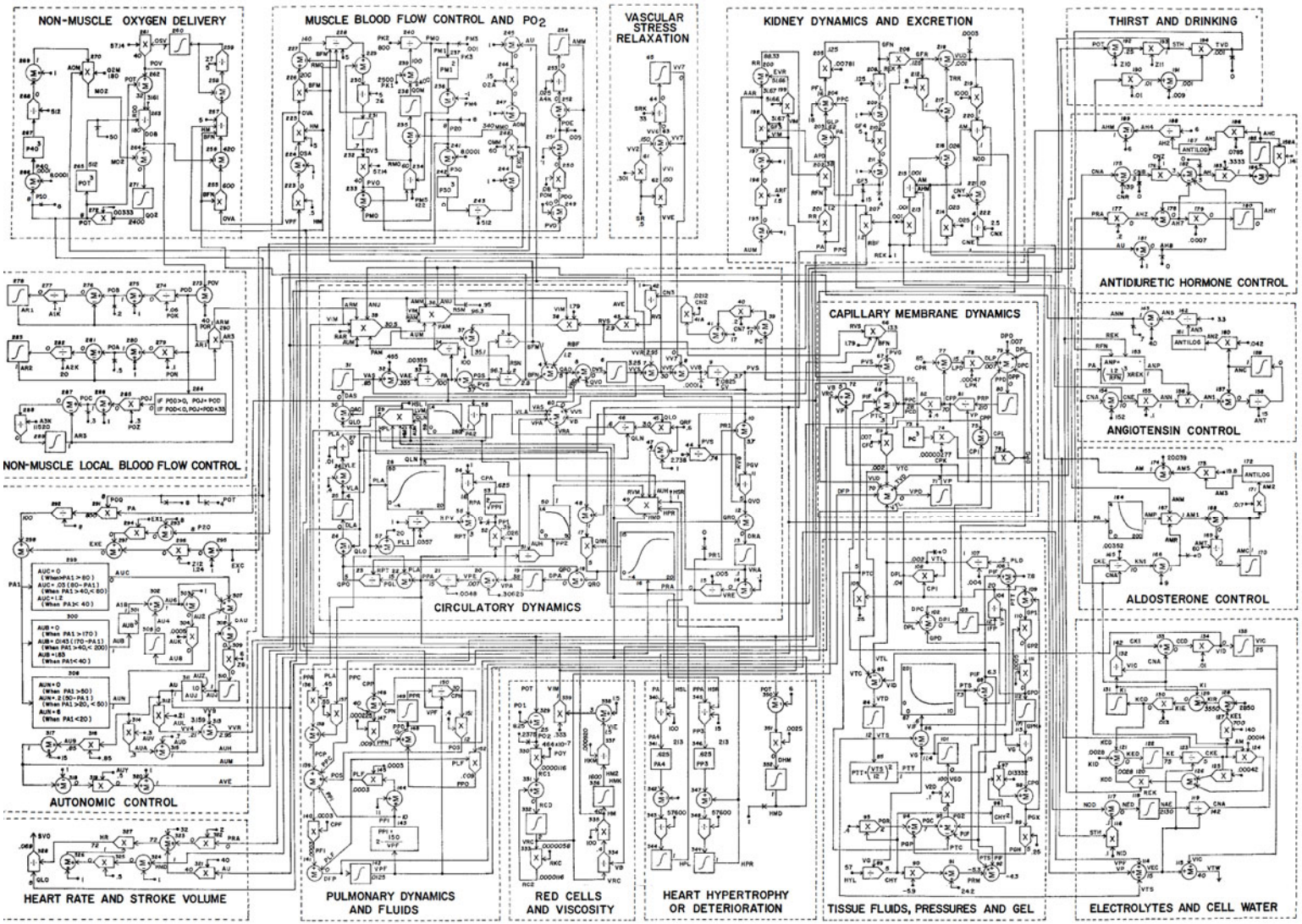
MPS cells regulate interstitial volume and blood pressure

Dr. Guyton‘s concept of overall circulation control



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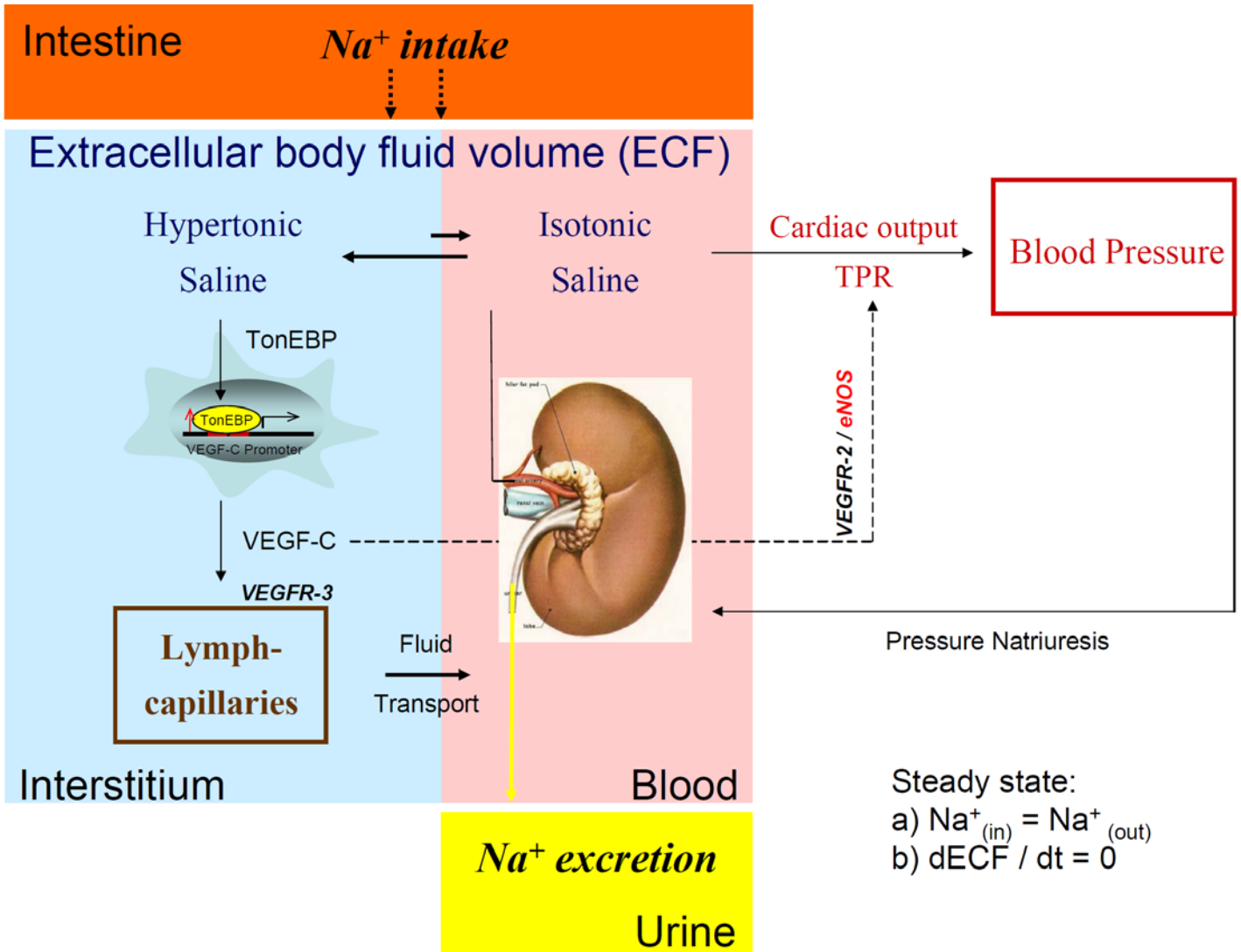

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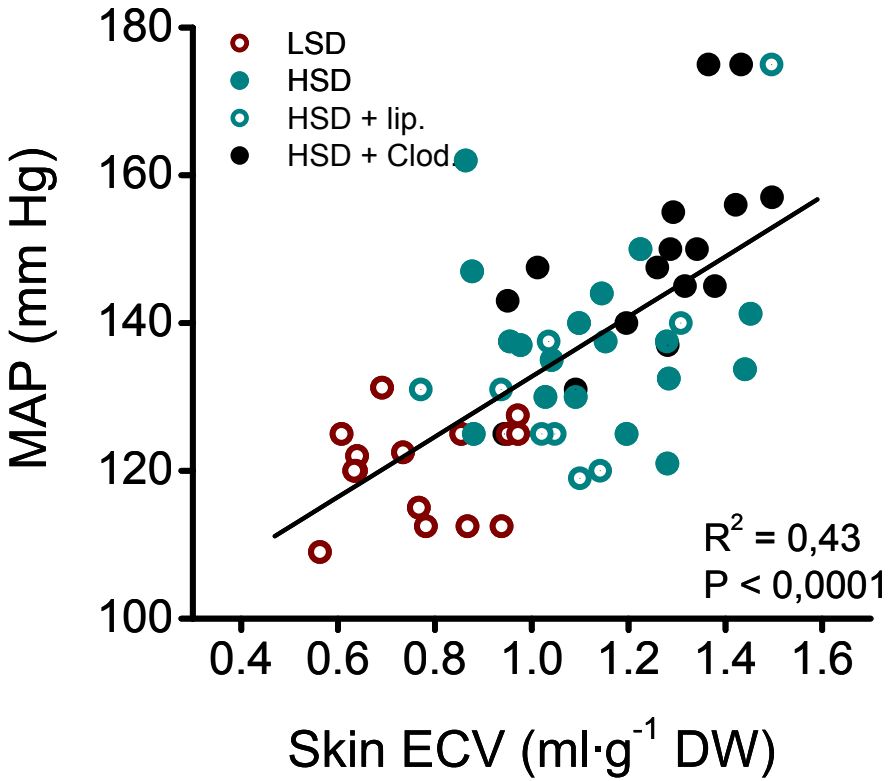

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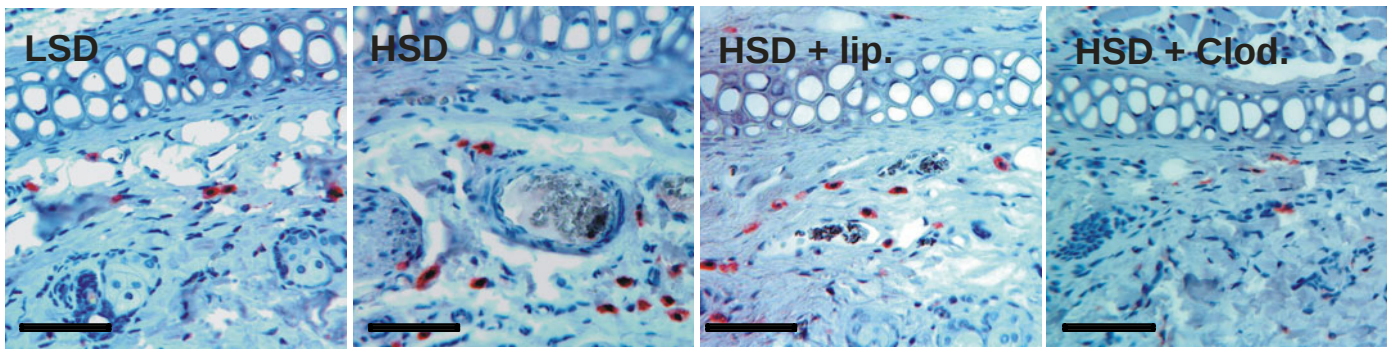
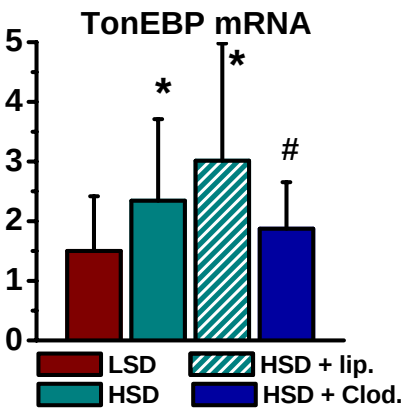
MPS cells and lymphatics: the system can be blocked

	LSD	HSD	HSD + lip.	HSD + Clod.
SK(Na^++K^+)/SKW	177 ± 8 mM	191 ± 7 * mM	187 ± 15 * mM	187 ± 10 * mM



Is MPS cell depletion paralleled by blocked TonEBP expression?



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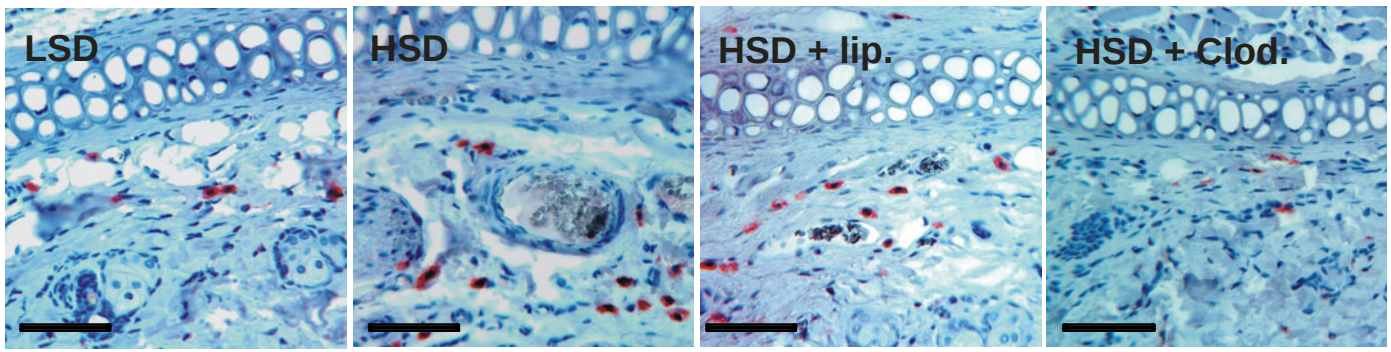

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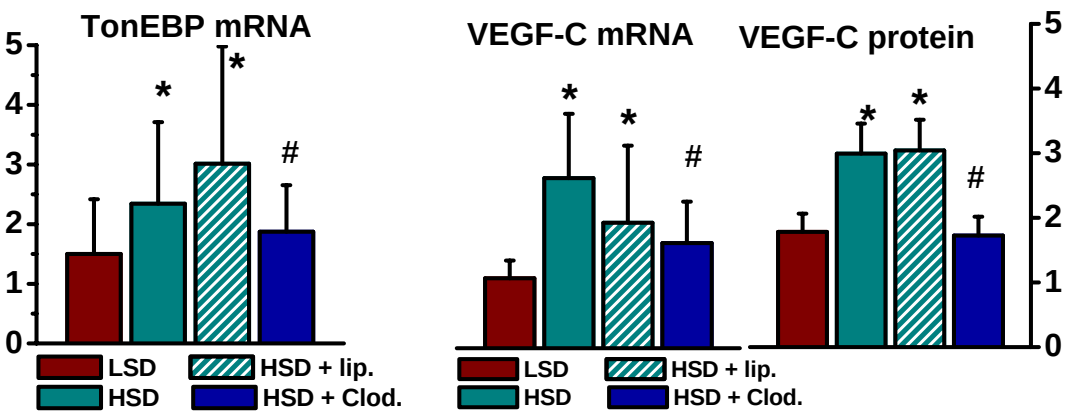

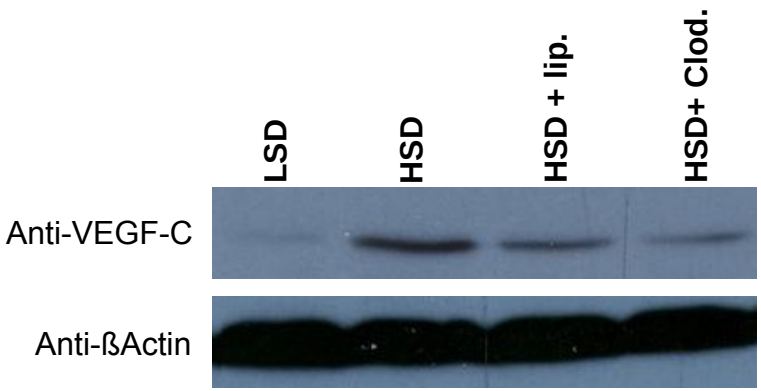

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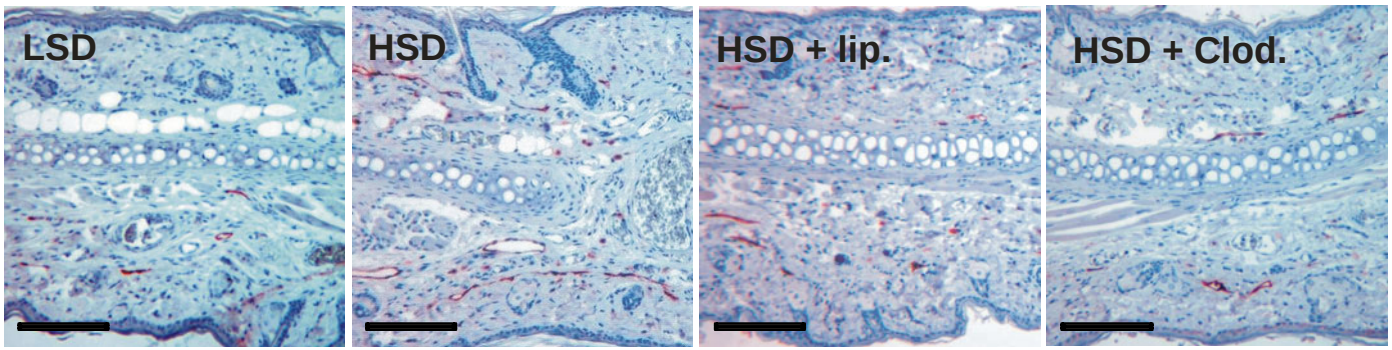
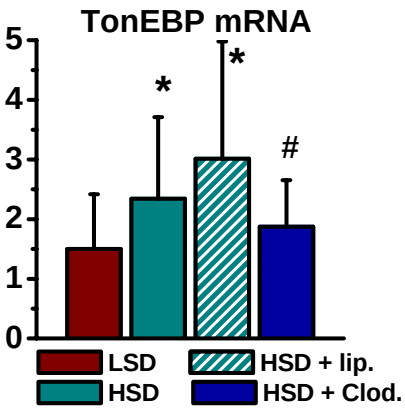
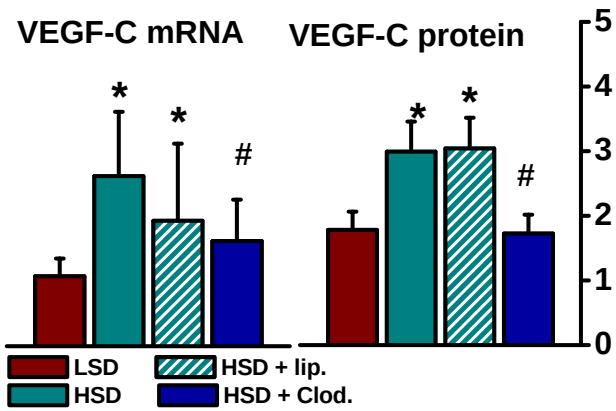
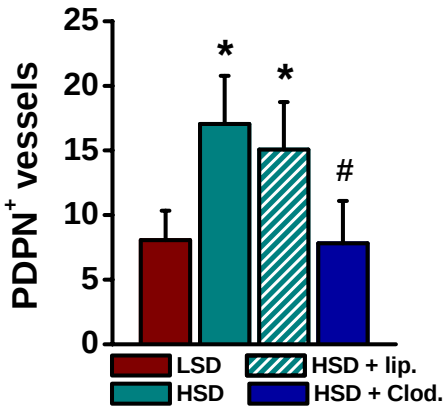


Is blocked VEGF-C expression paralleled by lymphcapillary hyperplasia?







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MPS cells and blood pressure regulation

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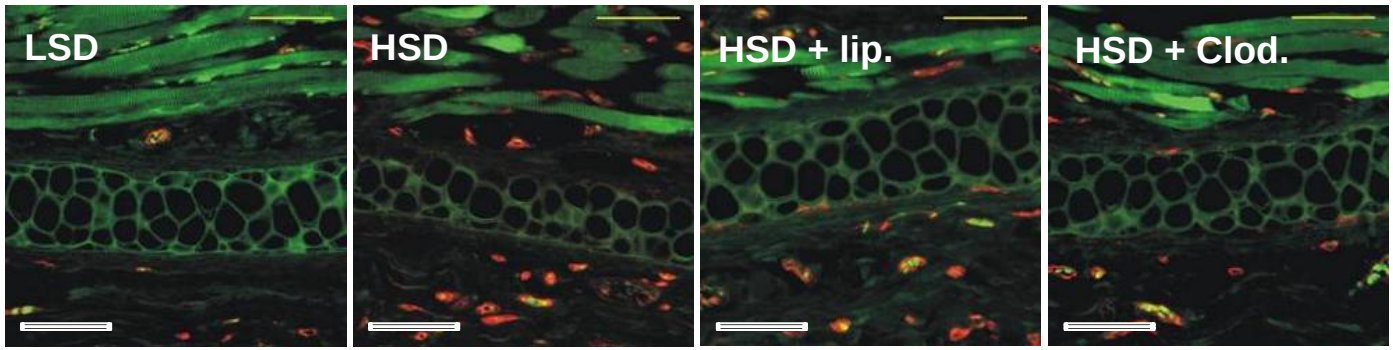

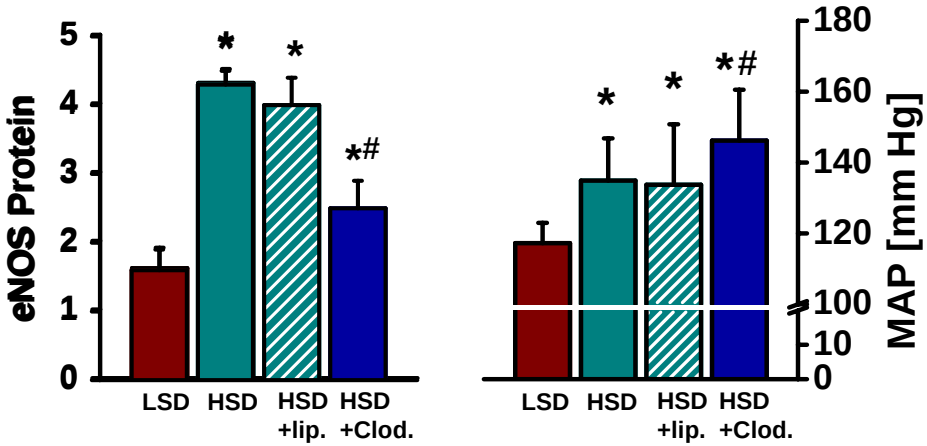

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But what about humans?

Salt and body Na^+ content in patients with refractory hypertension

Salt Intake and Hypertension

Effects of Dietary Sodium Reduction on Blood Pressure in Subjects With Resistant Hypertension

Results From a Randomized Trial

Eduardo Pimenta, Krishna K. Gaddam, Suzanne Oparil, Inmaculada Aban, Saima Husain, Louis J. Dell'Italia, David A. Calhoun

3.4 drugs / patient: hydrochlorothiazide, ACE-Blocker, AT1-receptor antagonist

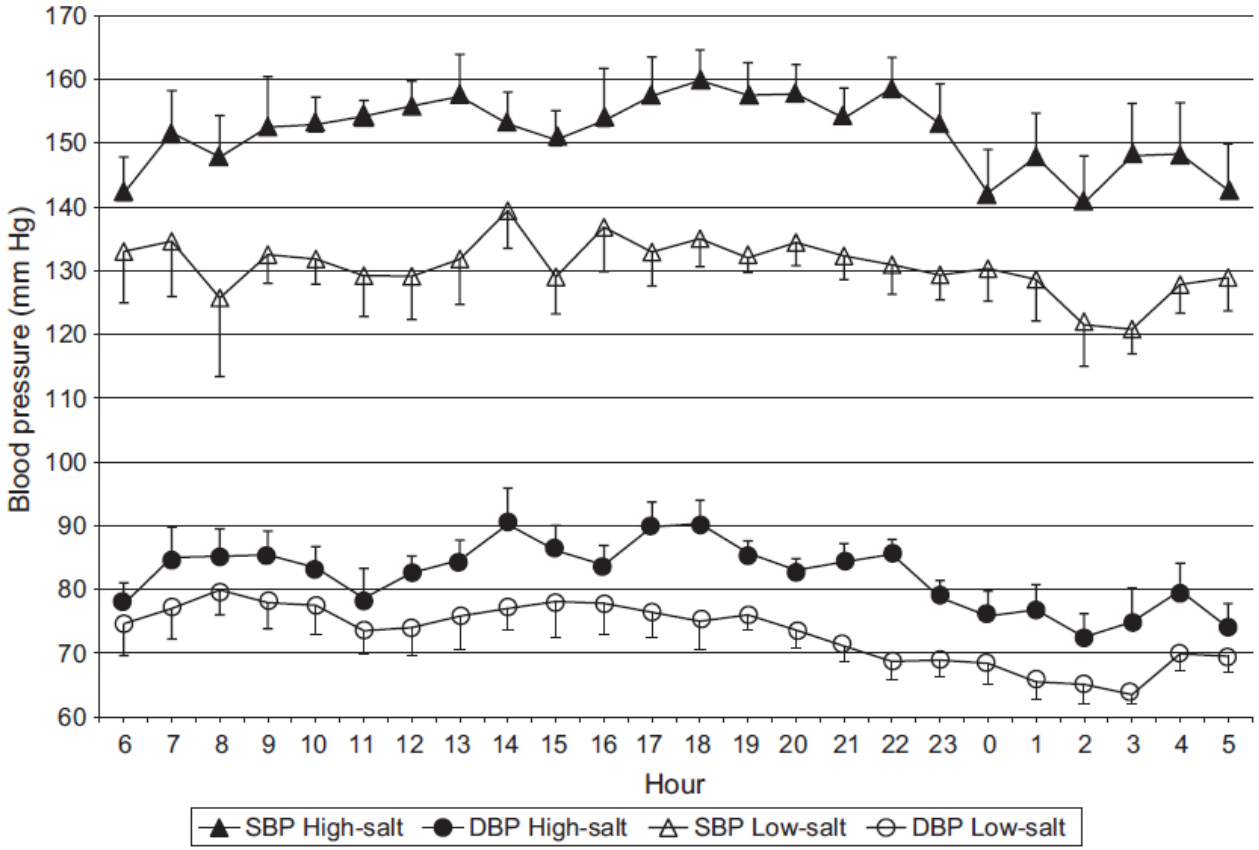
Hypertension 2009;54;475-481

Salt and body Na^+ content in patients with refractory hypertension

	2 weeks „regular“ diet	1 week low-salt diet
Urinary Na^+ (mmol / day)	252.2 ± 64.6	46.1 ± 26.8
Urinary Aldo (mcg / day)	11.7 ± 5.1	16.5 ± 7.9
Plasma Renin (ng/ml/h)	0.6 ± 0.7	2.7 ± 15.2

Hypertension 2009;54;475-481

Salt and body Na^+ content in patients with refractory hypertension

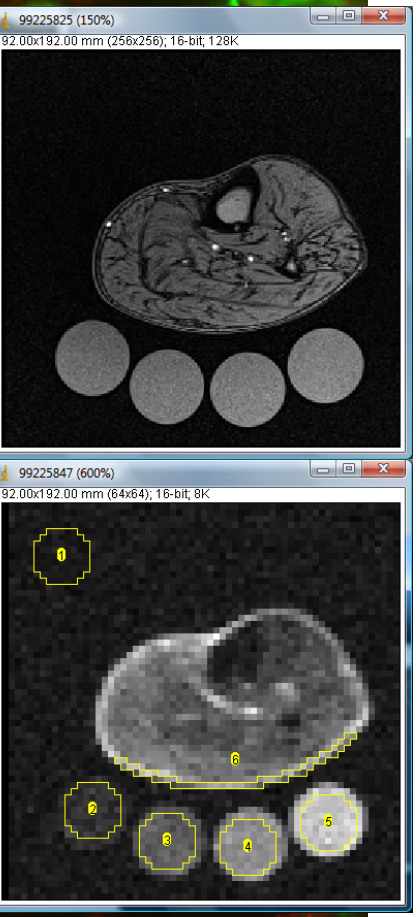


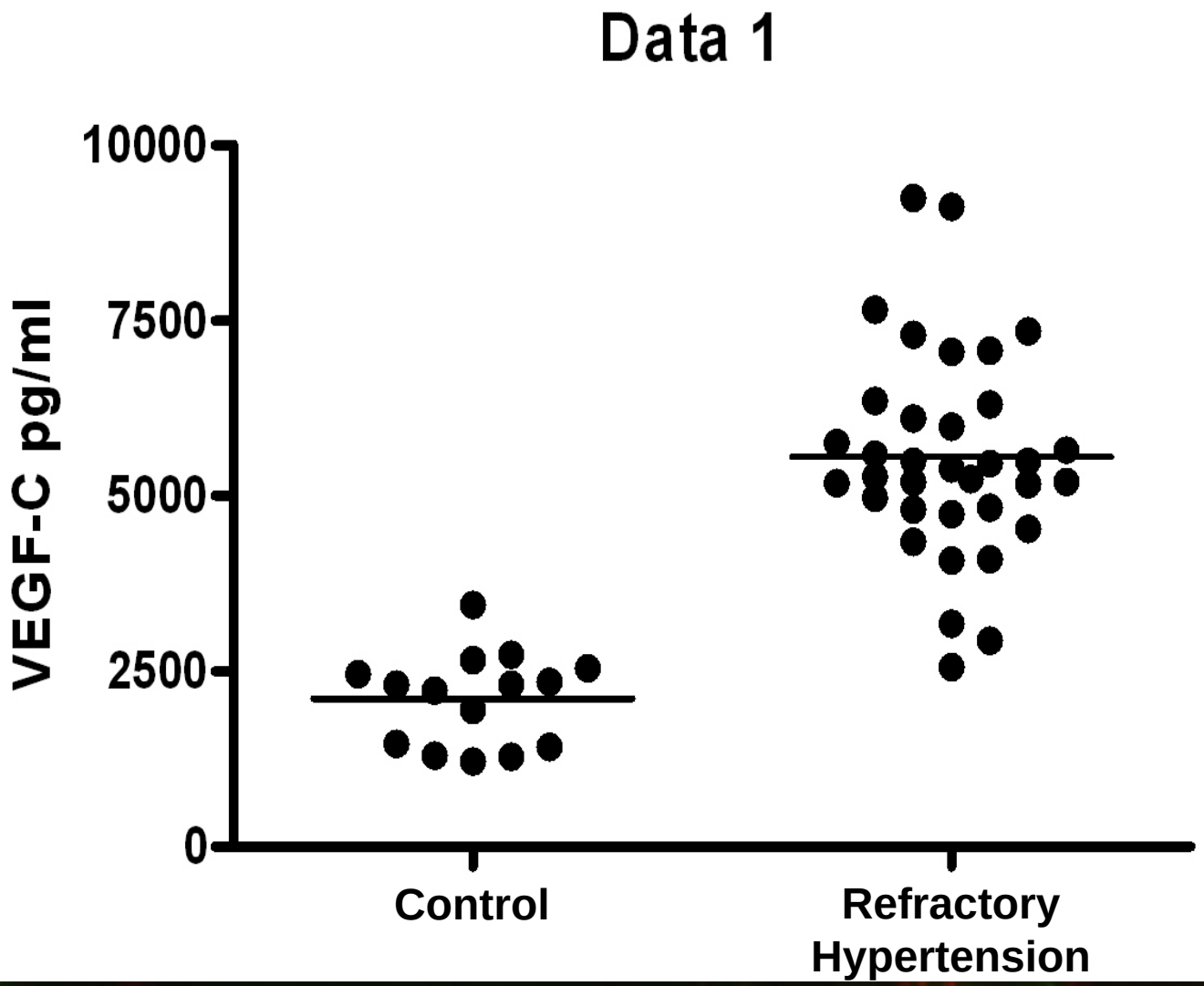
- 20.1 mmHg

- 9.8 mmHg

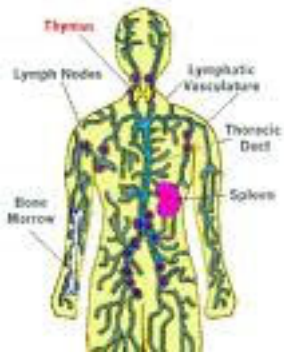
Hypertension 2009;54;475-481

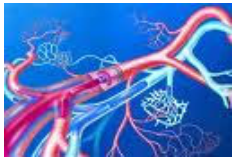
Can we translate?

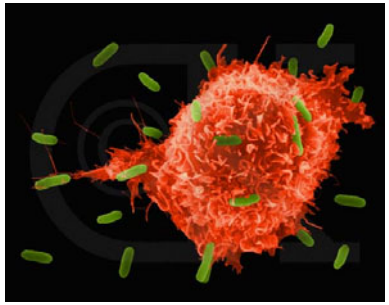




The constantocentric (blood) and variable (interstitium) world





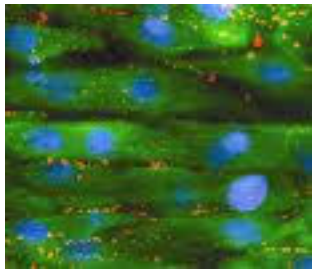


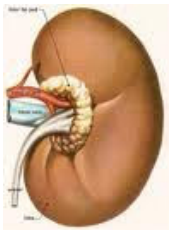
Constancy of the internal environment:

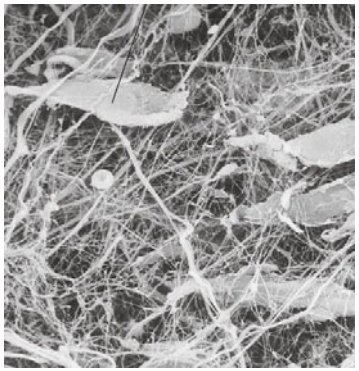
- content
- concentrations

Variability of the internal environment:

- content
- concentrations







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