The Role of T Cells in the Pathogenesis of Hypertension Part 2.

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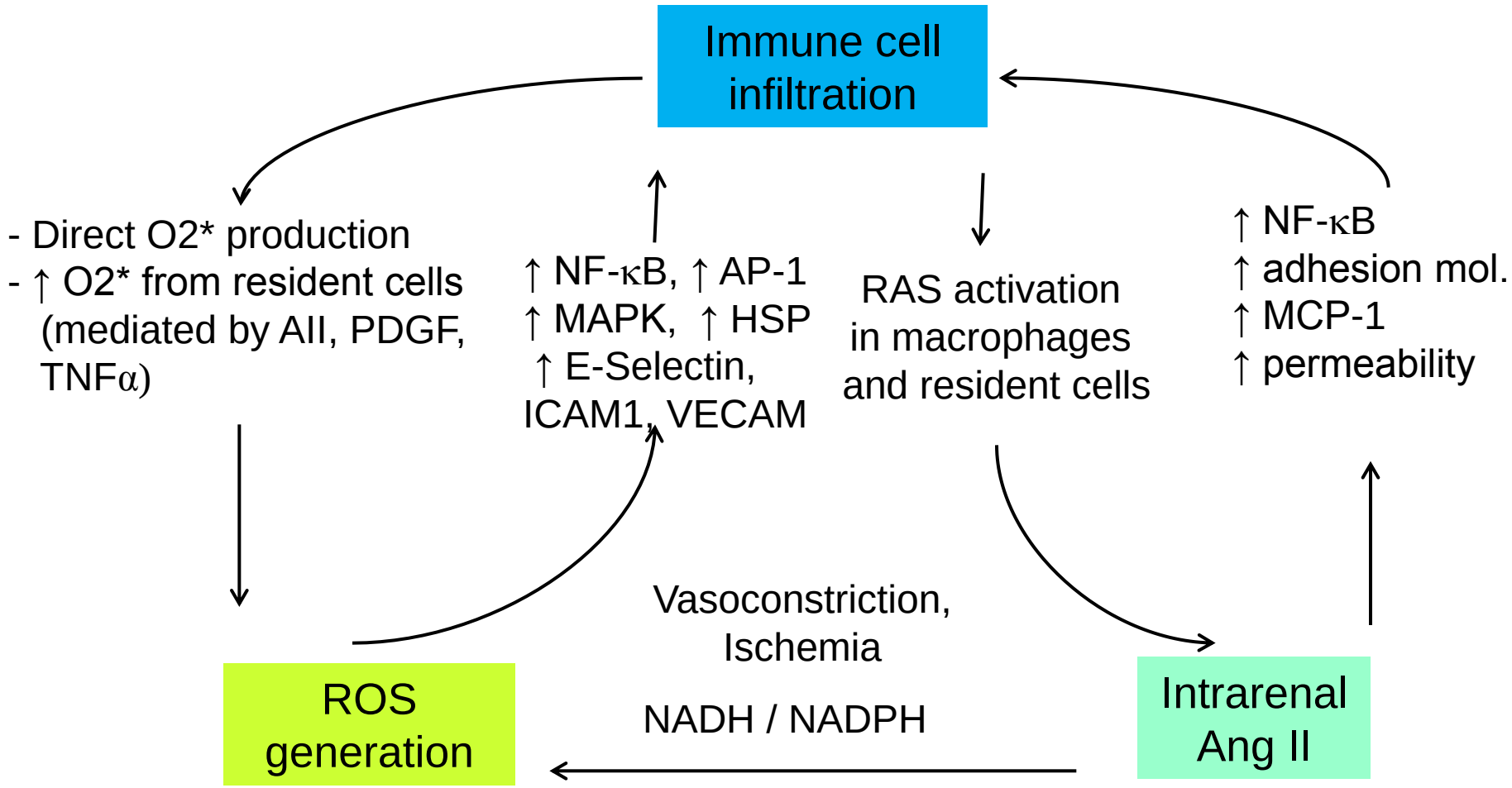
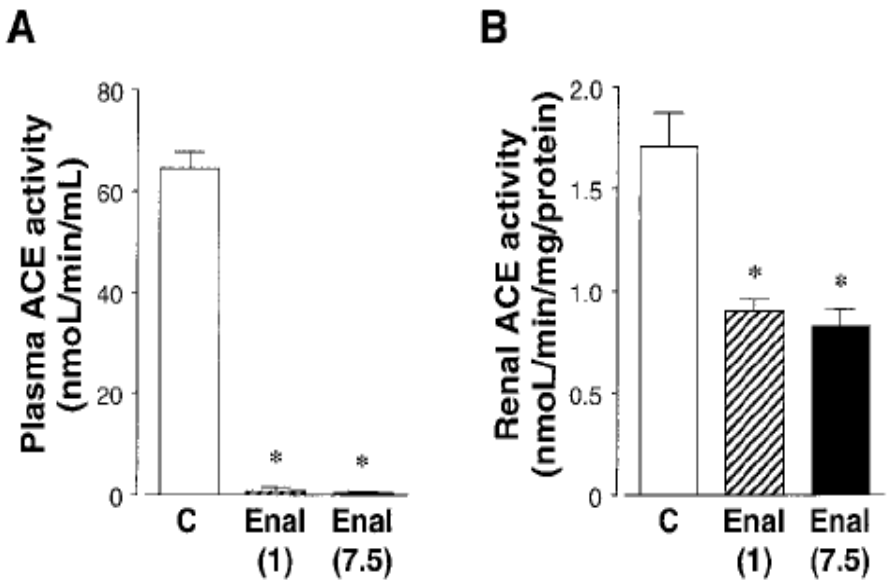


Vaziri ND, Rodriguez-Iturbe B. *Nature Clin Prac Nephrol*, 2006

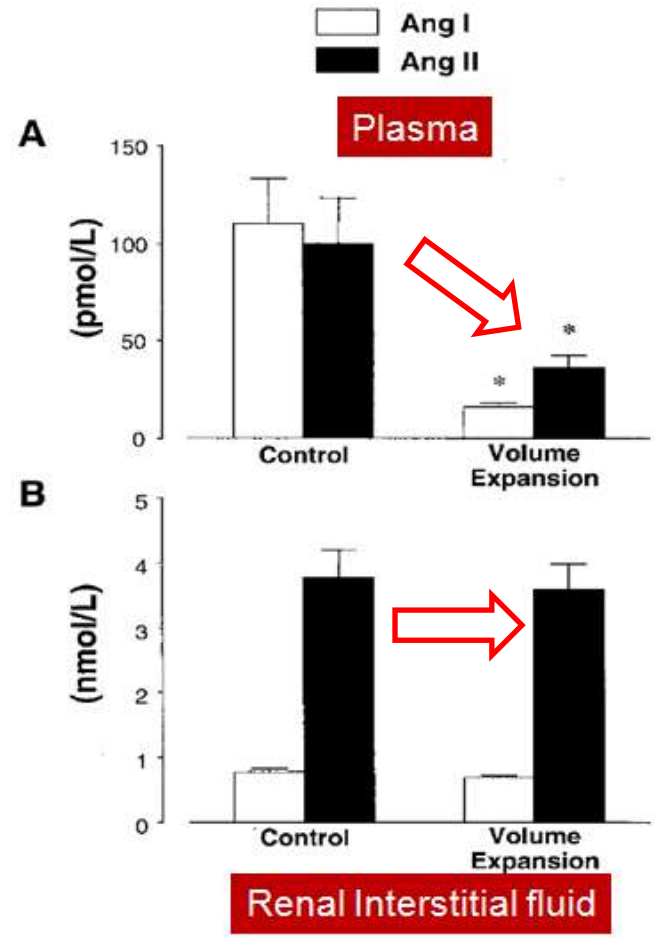
Renal and plasma angiotensin activity do not have the same physiological modulation

Less suppression by ACEI

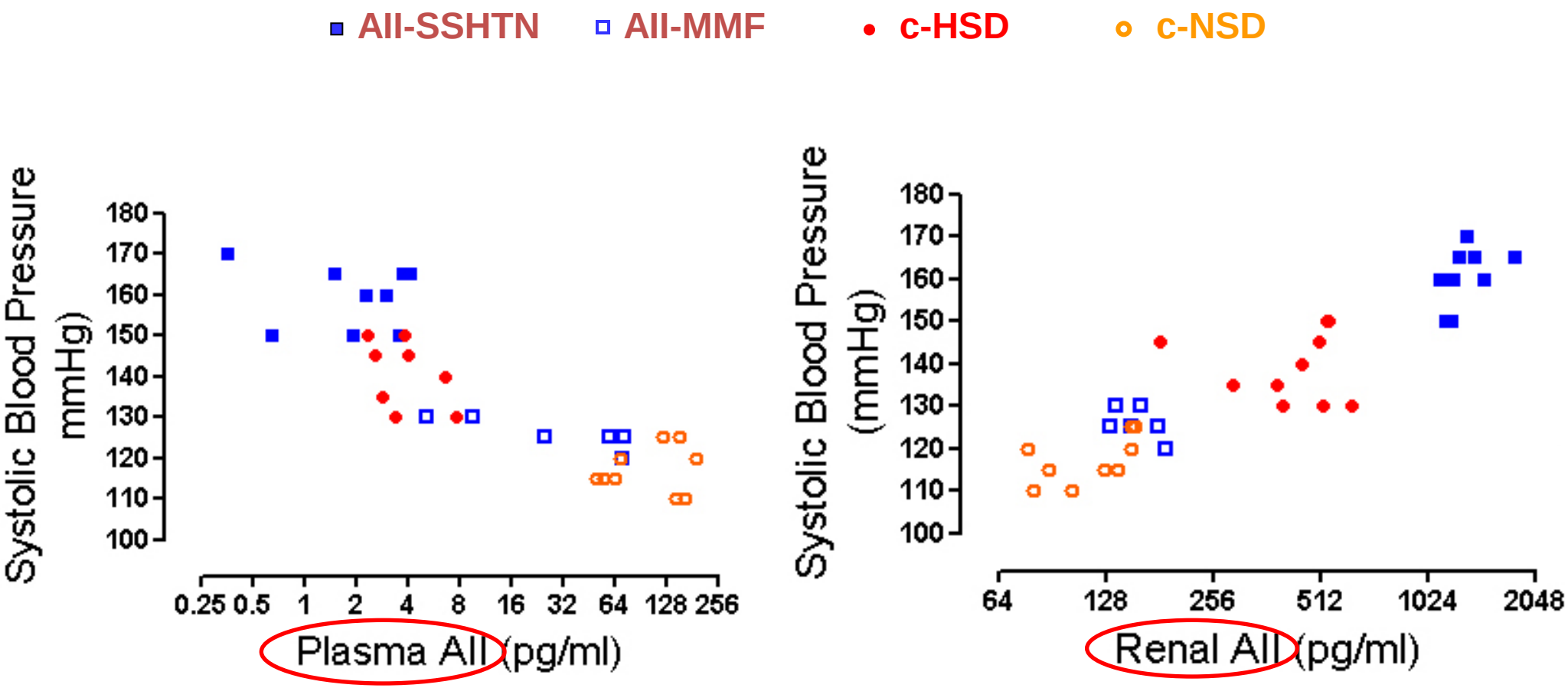


Nishiyama A, Seth DM, Navar G. Hypertension 2002; 39:129-34

Lack of suppression by plasma expansion



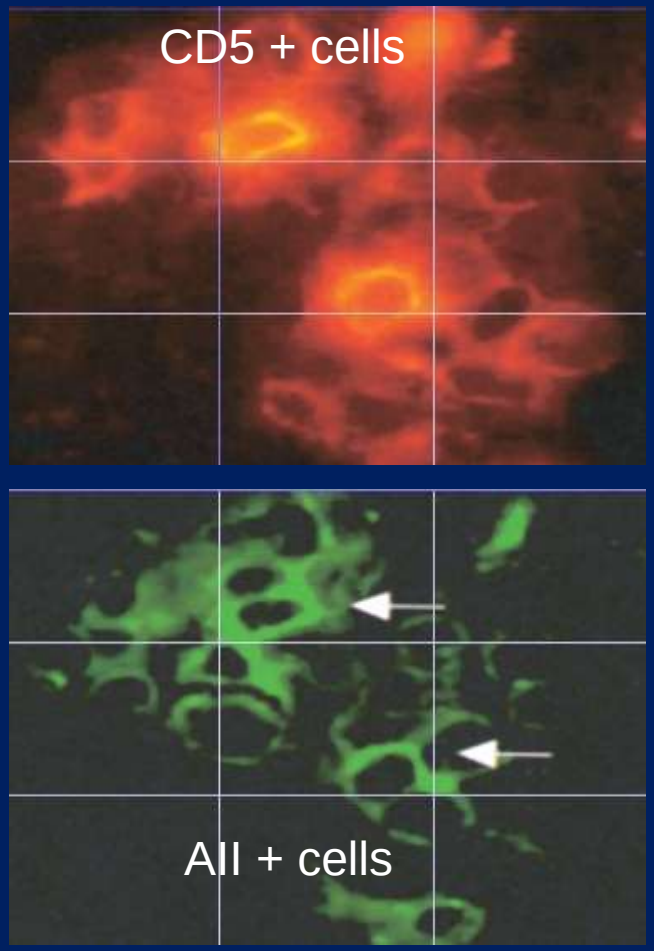
In AII-induced SSHTN hypertension, plasma and renal AII *independent* and may be modified in *oposite* directions



Am J Physiol Regul Integr Comp Physiol 293: R251–R256, 2007.

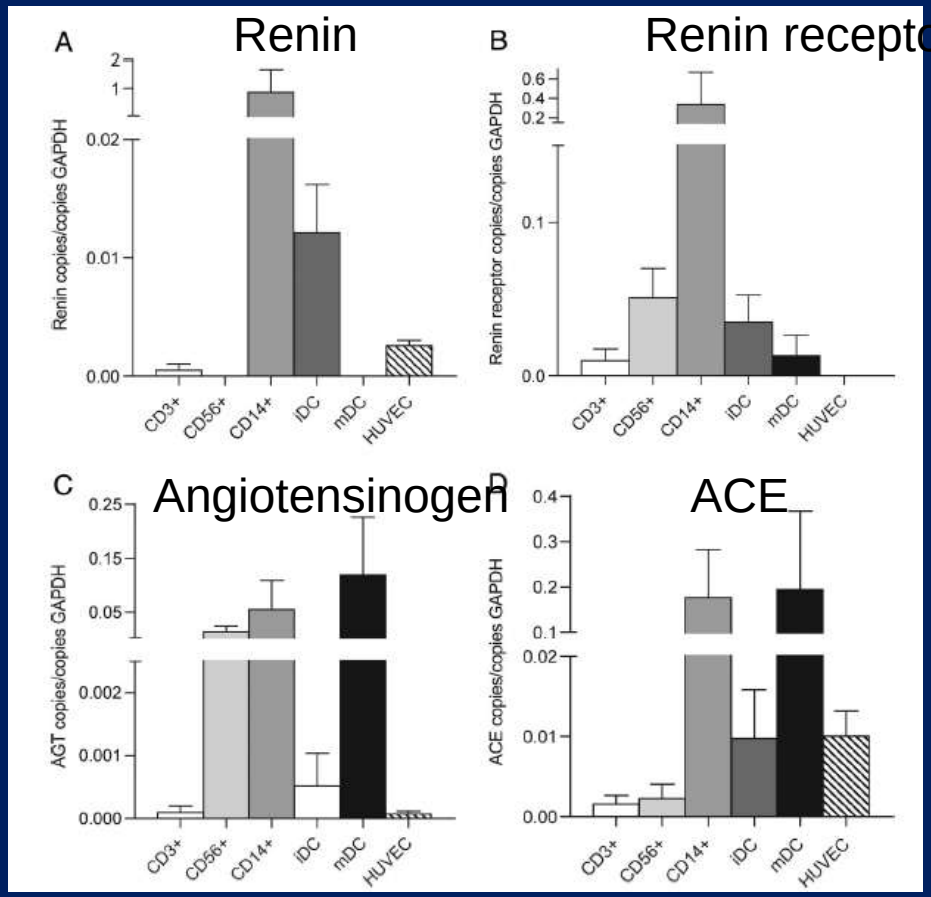
LYMPHOCYTES PRODUCE ANGIOTENSIN II

Double staining studies



Kidney Int 2001;59:2222-32

RAS components in lymphocytes

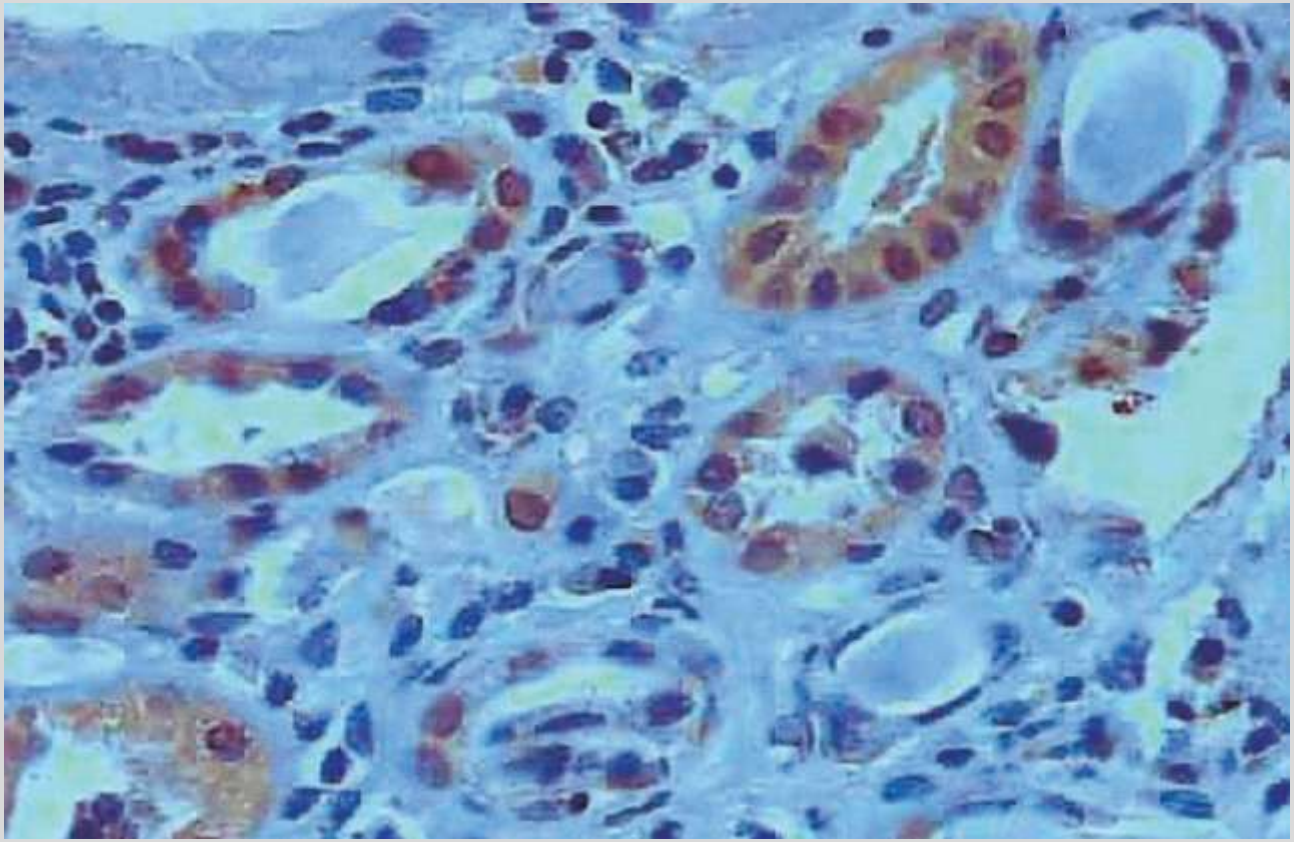


Jurewicz M et al. *J Am Soc Nephrol* 18: 1093–1102, 2007.

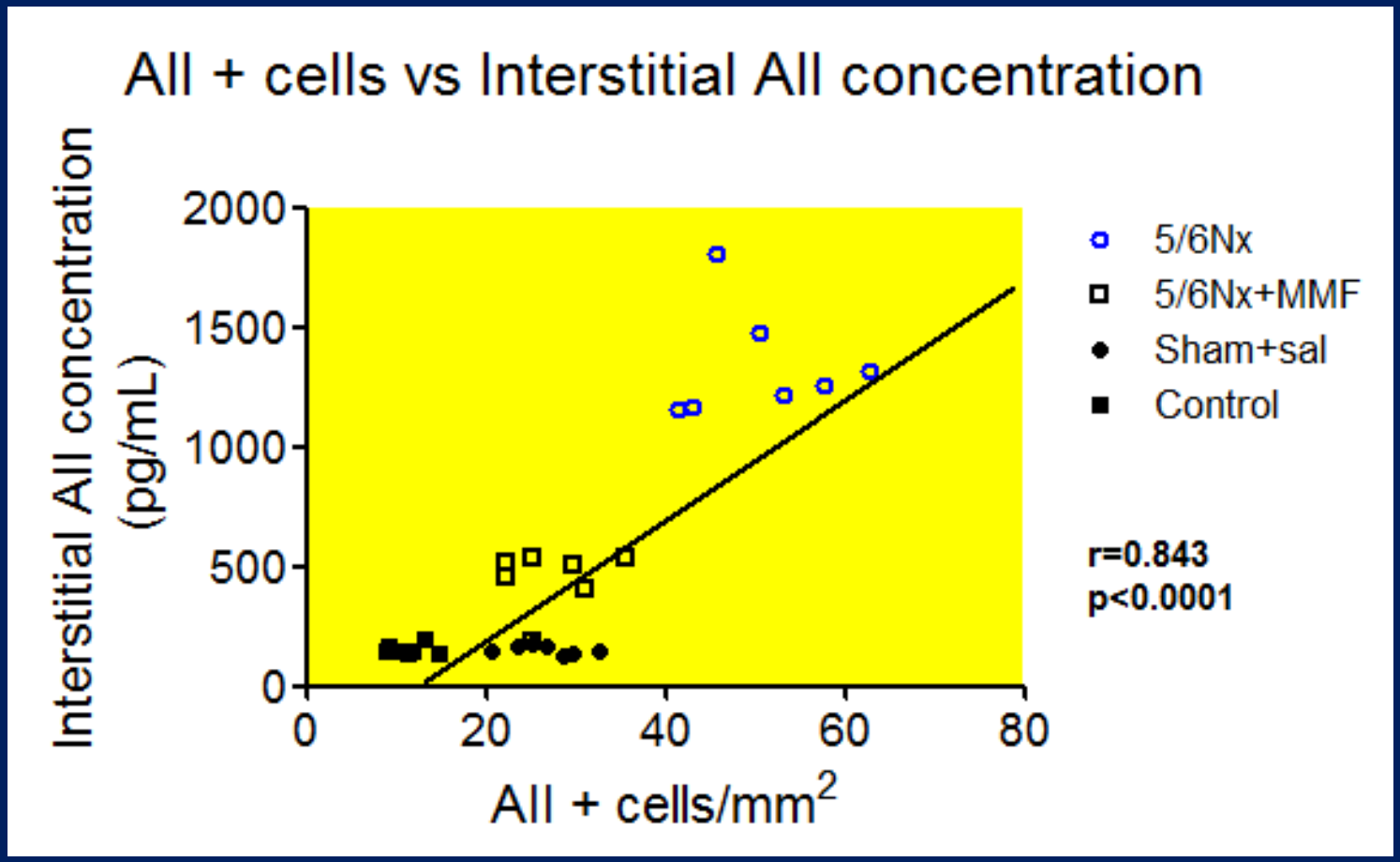
HUMANS Ang II positive cells are tubular cells and infiltrating interstitial cells

Oxidative stress, renal infiltration of immune cells, and salt-sensitive hypertension: all for one and one for all *Am J Physiol Renal Physiol* 286: F606–F616, 2004

Bernardo Rodríguez-Iturbe,[1] Nosratola D. Vaziri,[2] Jaime Herrera-Acosta,[3] and Richard J. Johnson[4]



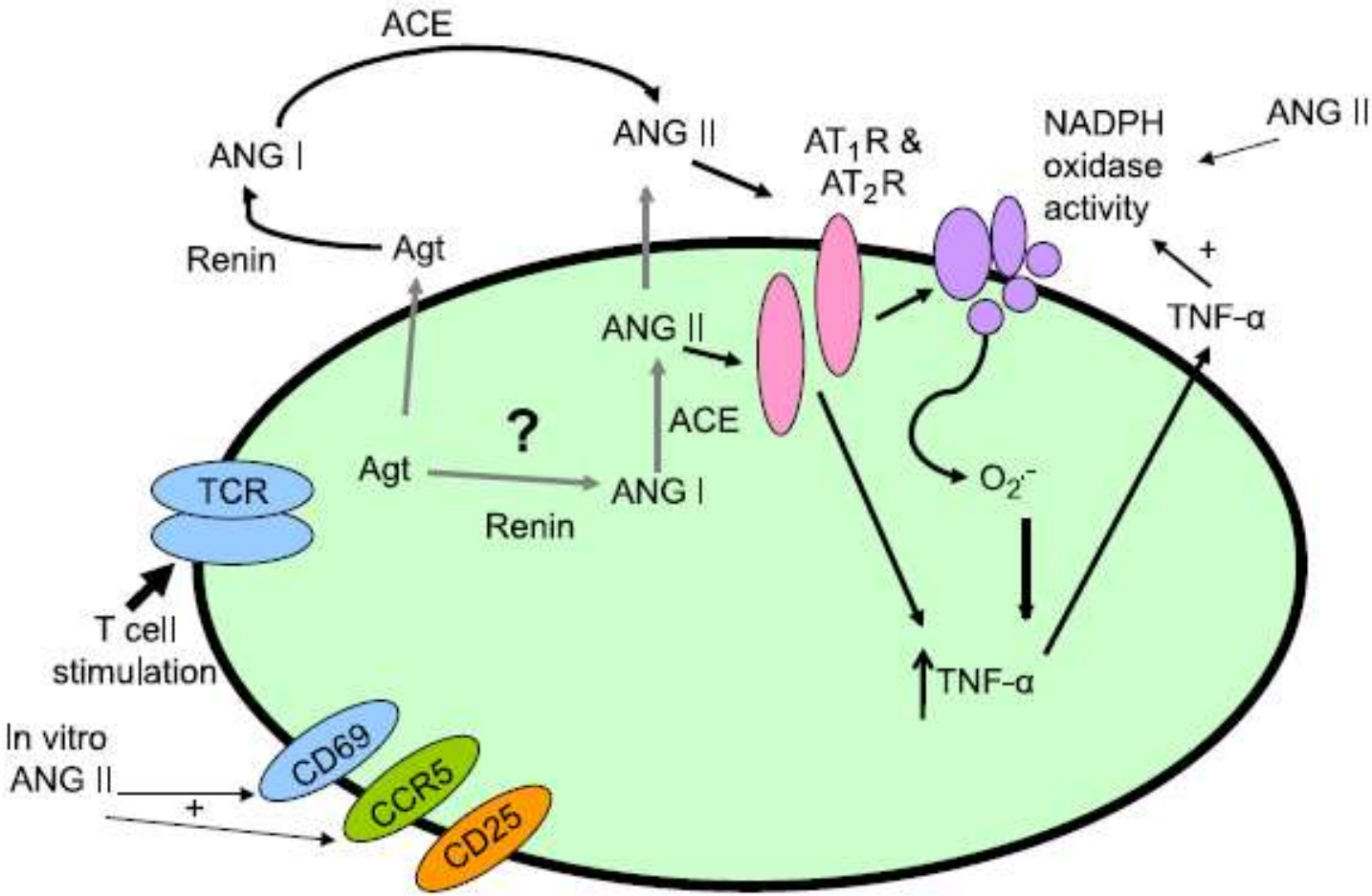
Courtesy Sergio Mezzano

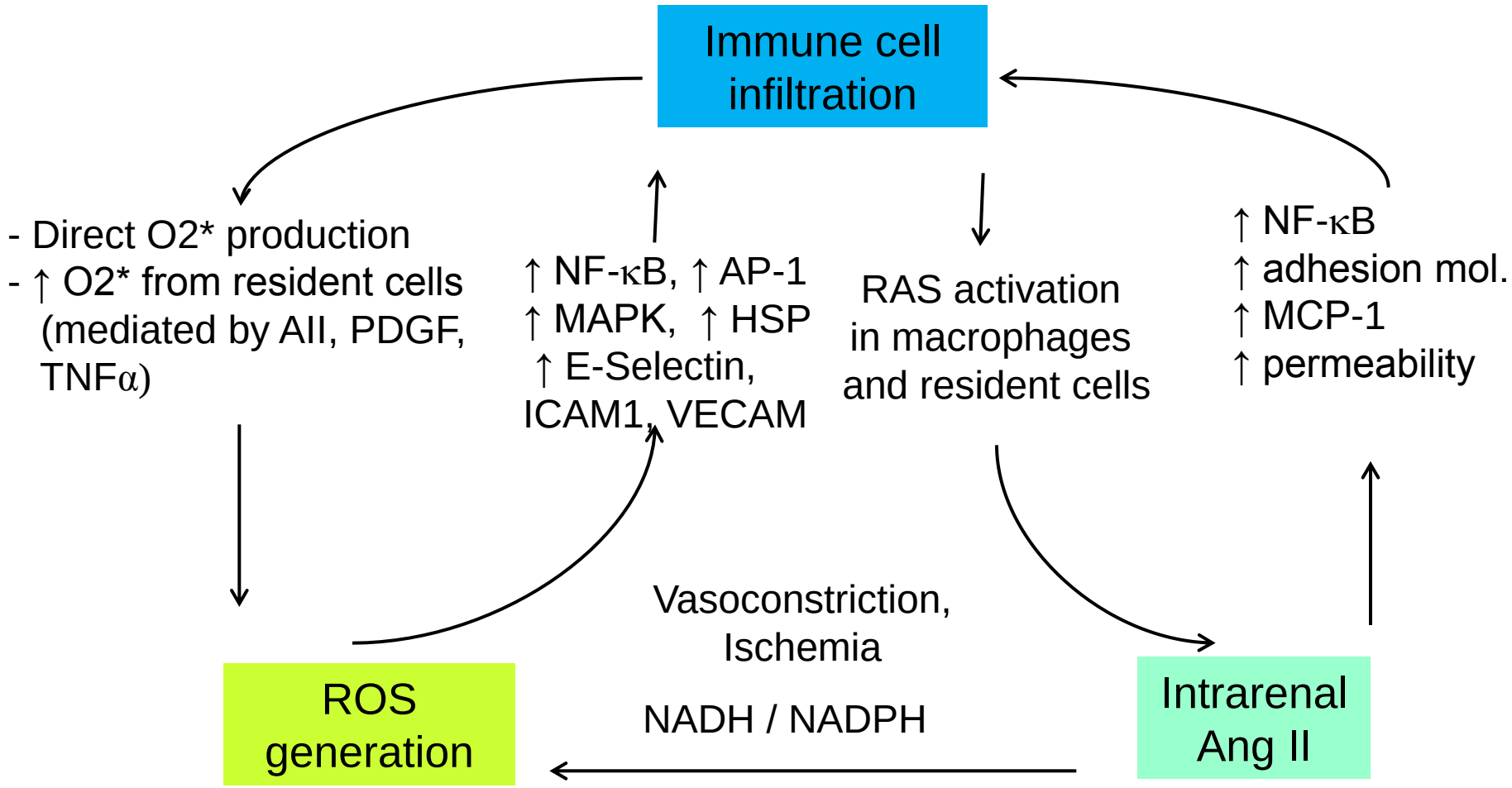


Franco M et al. 2007

Endogenously produced angiotensin II regulates T cell function

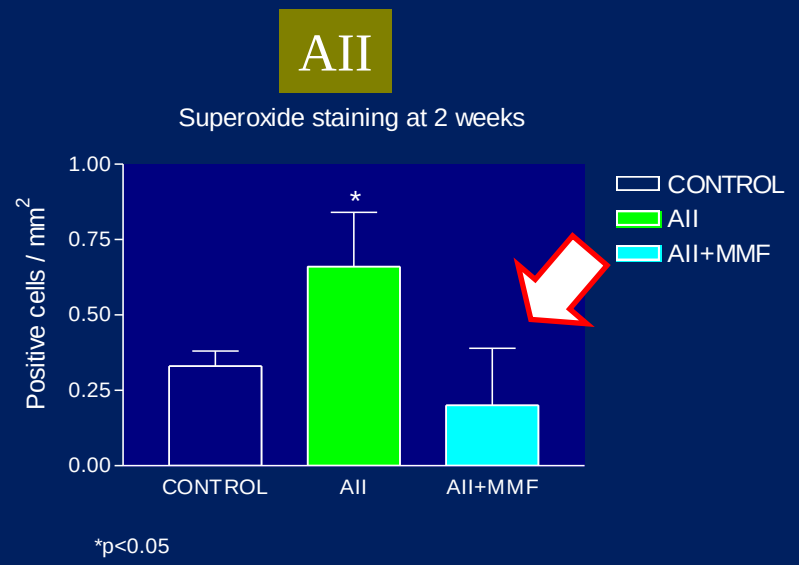
Hotch et al. (2009). Endogenously produced AII regulates T cell function *AJP Reg 296:208-216,*

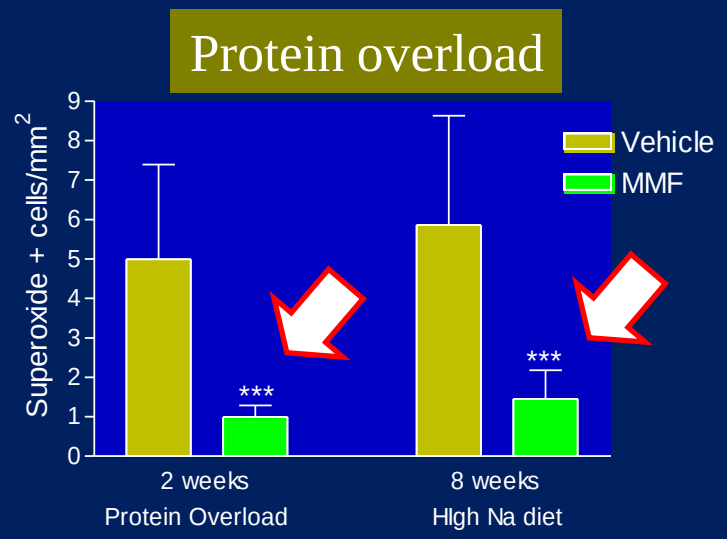


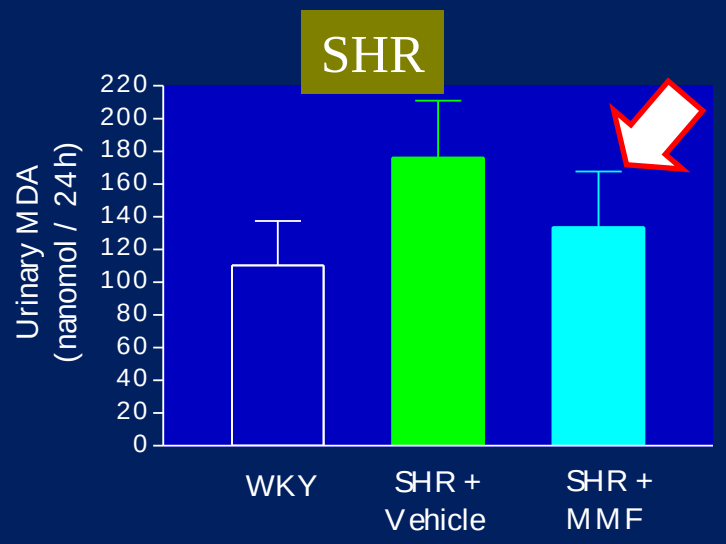


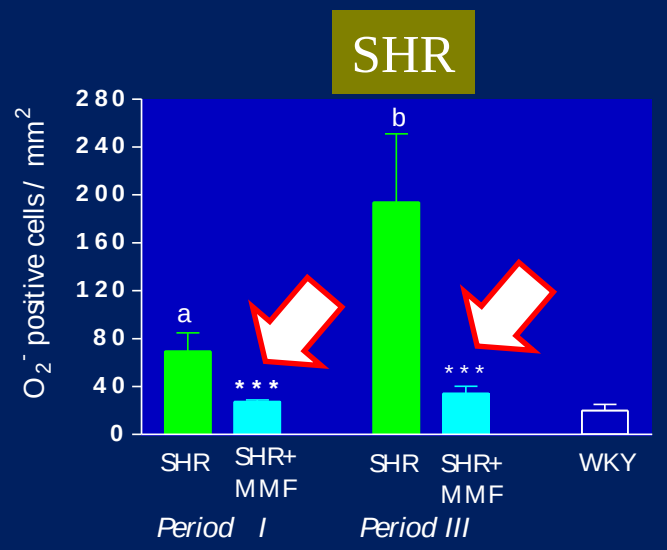
Vaziri ND, Rodriguez-Iturbe B. *Nature Clin Prac Nephrol*, 2006

Reduction of inflammatory infiltration reduces oxidative stress

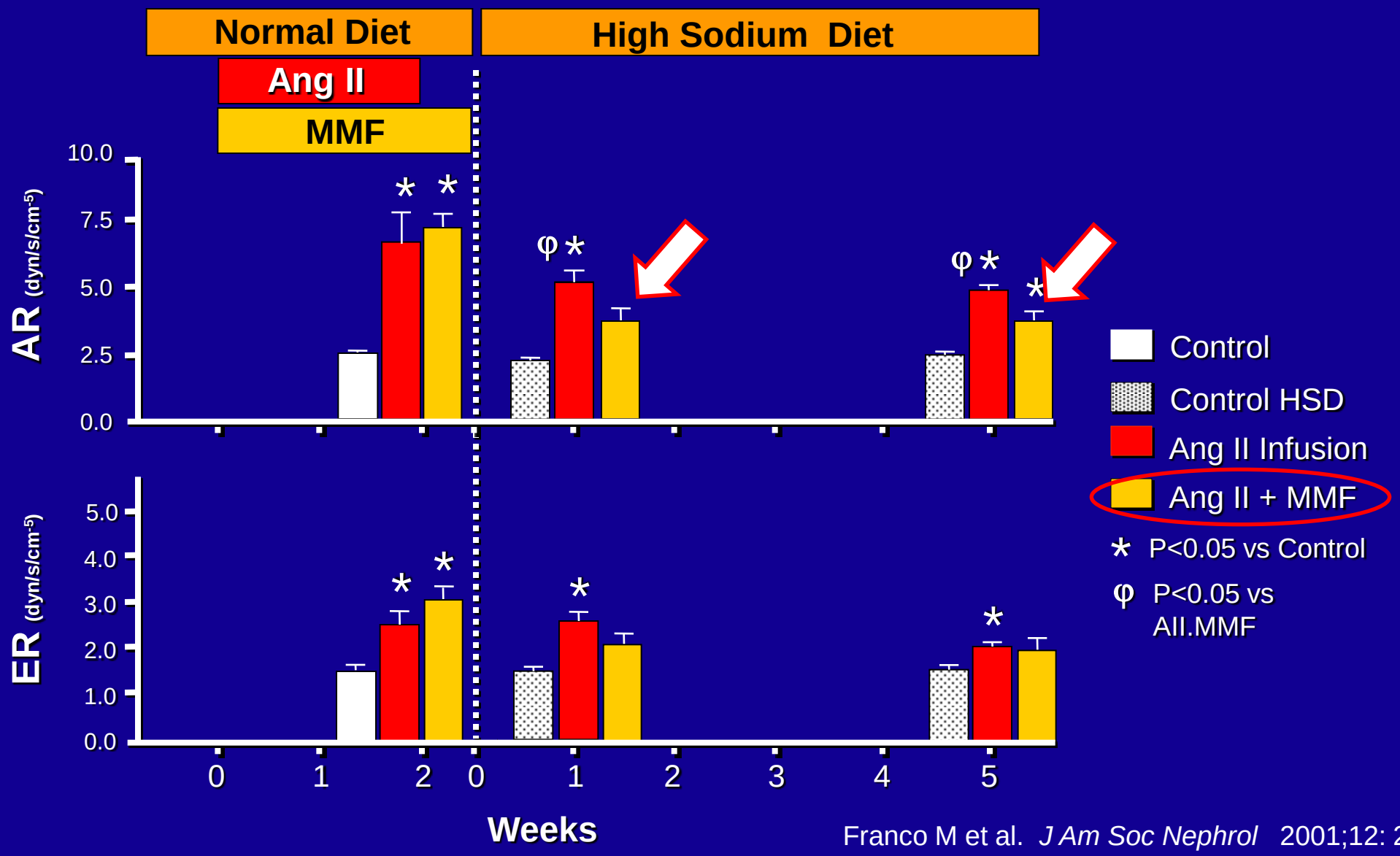








Glomerular Hemodynamics in SSHTN induced by Ang II. Effects of MMF



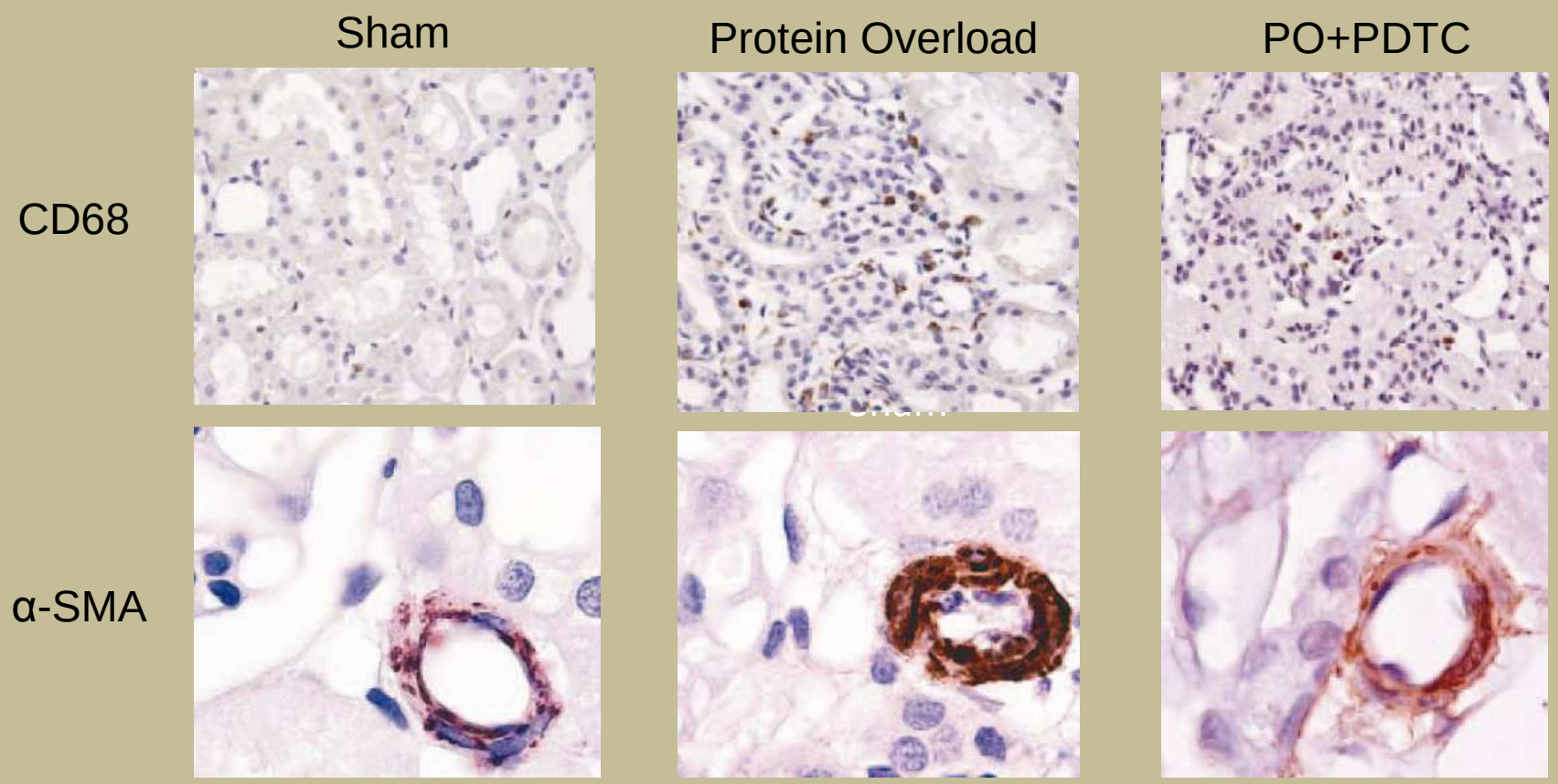
Franco M et al. *J Am Soc Nephrol* 2001;12: 2263-71

Preglomerular arteriolar hypertrophy associated with TI inflammation-induced hypertension

Treatment with pyrrolidine dithiocarbamate improves proteinuria, oxidative stress, and glomerular hypertension in overload proteinuria

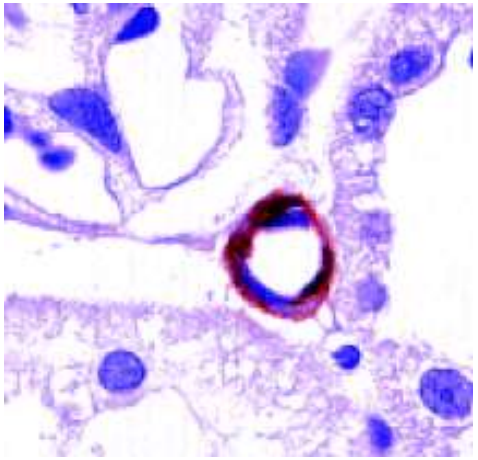
Edilia Tapia,[1] Dolores J. Sánchez-González,[4] Omar N. Medina-Campos,[6] Virgilia Soto,[2] Carmen Ávila-Casado,[2] Claudia M. Martínez-Martínez,[4] Richard J. Johnson,[3] Bernardo Rodríguez-Iturbe,[5] José Pedraza-Chaverrí,[6] Martha Franco,[1] and Laura G. Sánchez-Lozada[1]

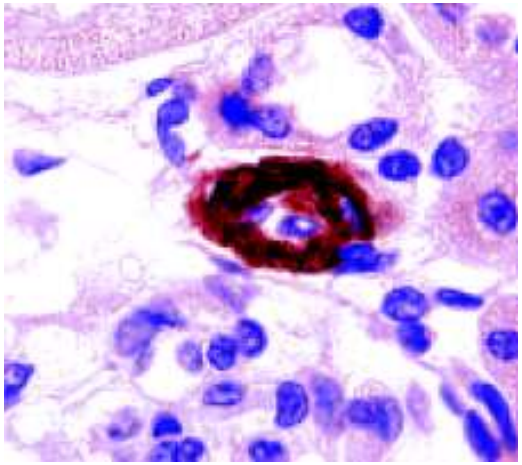
Am J Physiol Renal Physiol 295: F1431–F1439, 2008.

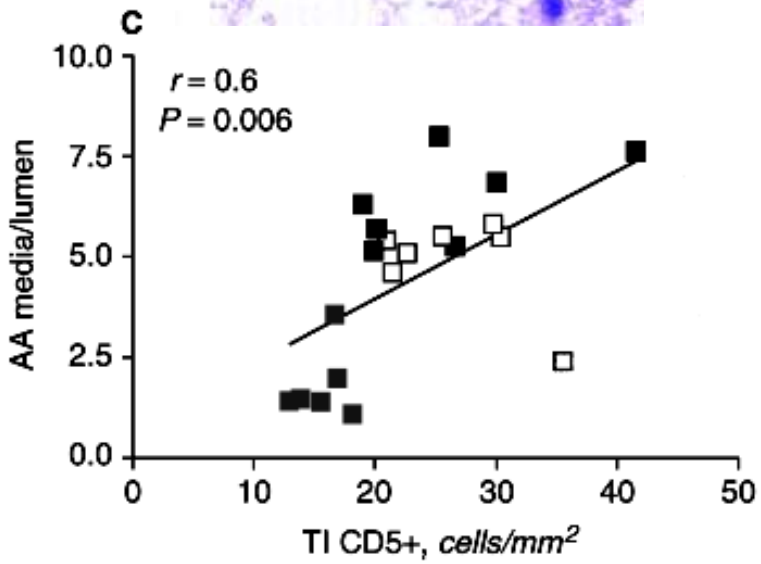


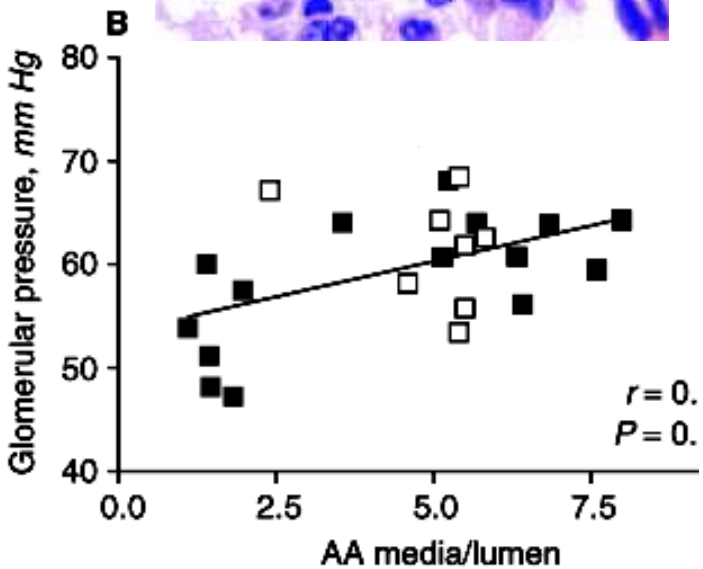
Afferent arteriolar vasoconstriction and remodeling induced by tubulointerstitial inflammation

Herrera-Acosta J et al.







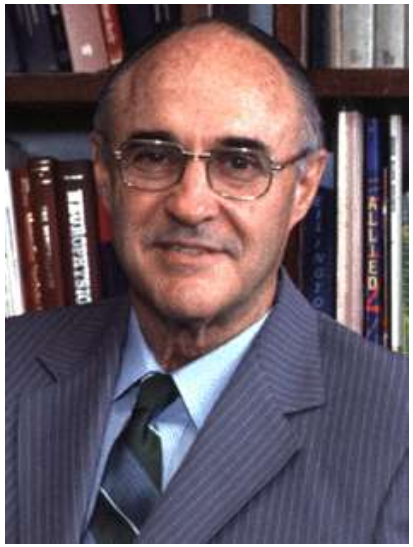


Kidney Int. 67:237-47, 2005 **Kidney Int 63:994, 2003** **Kidney Int 64 (Suppl 86) s9-s14, 2003**

Koranyi S. (1866-1944)

(when) the kidneys lose capacity, the function can be maintained by recruiting compensating mechanisms, so that a new balanced steady state ensues.

Koranyi S. Physikalisch-chemische Methoden und Gesichtspunkte in ihrer Anwendung auf die pathologische Physiologje des Kreislaufes, Z *Physiol 1897*



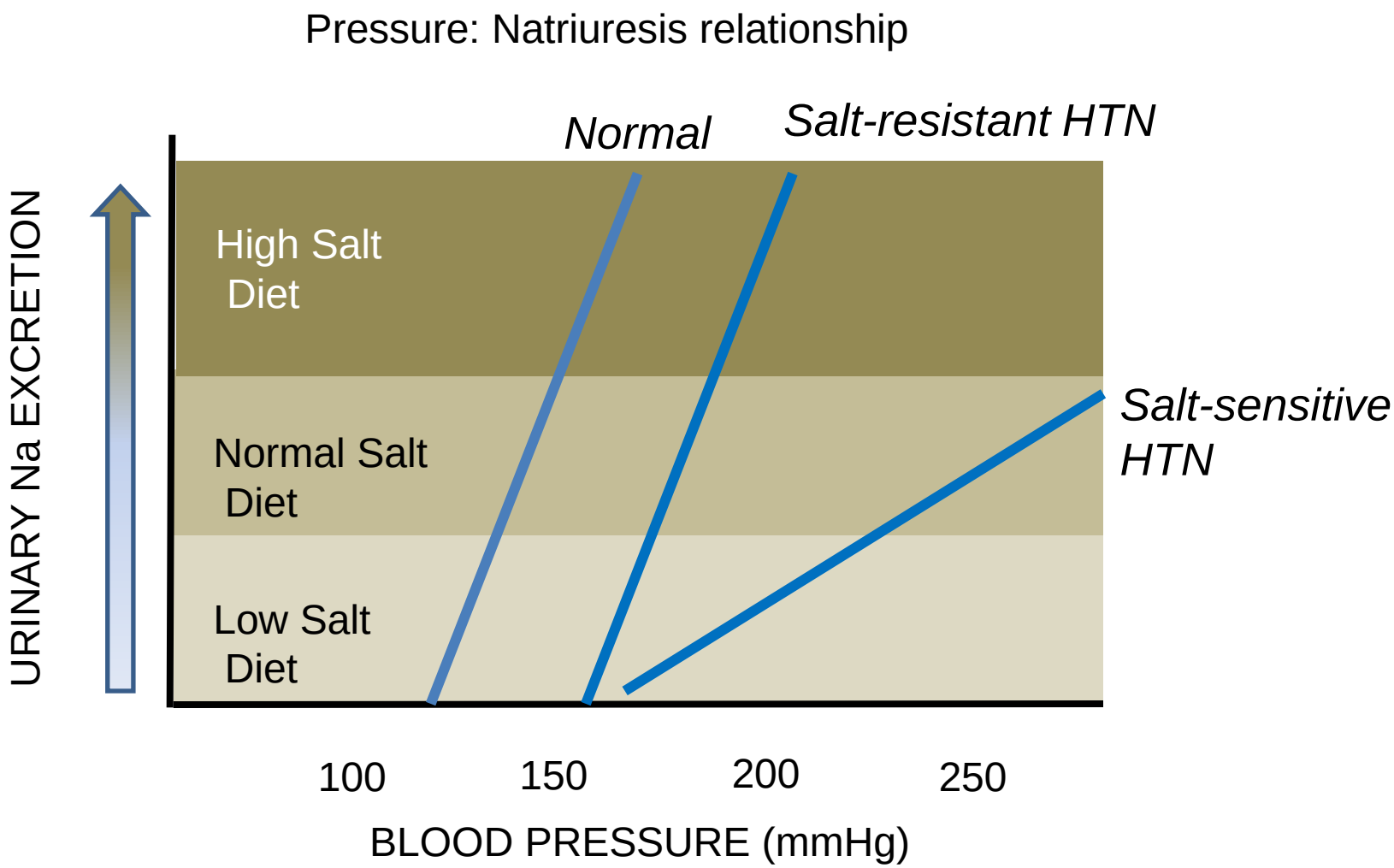
Guyton AC (1919-2003)

The basic cause of essential hypertension is the inability of the kidneys to excrete an adequate volume of urine at normal arterial pressure. Therefore, fluid accumulates in the body until the pressure rises high enough to balance fluid output with fluid intake

Hypertension is a compensatory response to maintain sodium and fluid balance when there is impairment in sodium and fluid excretion

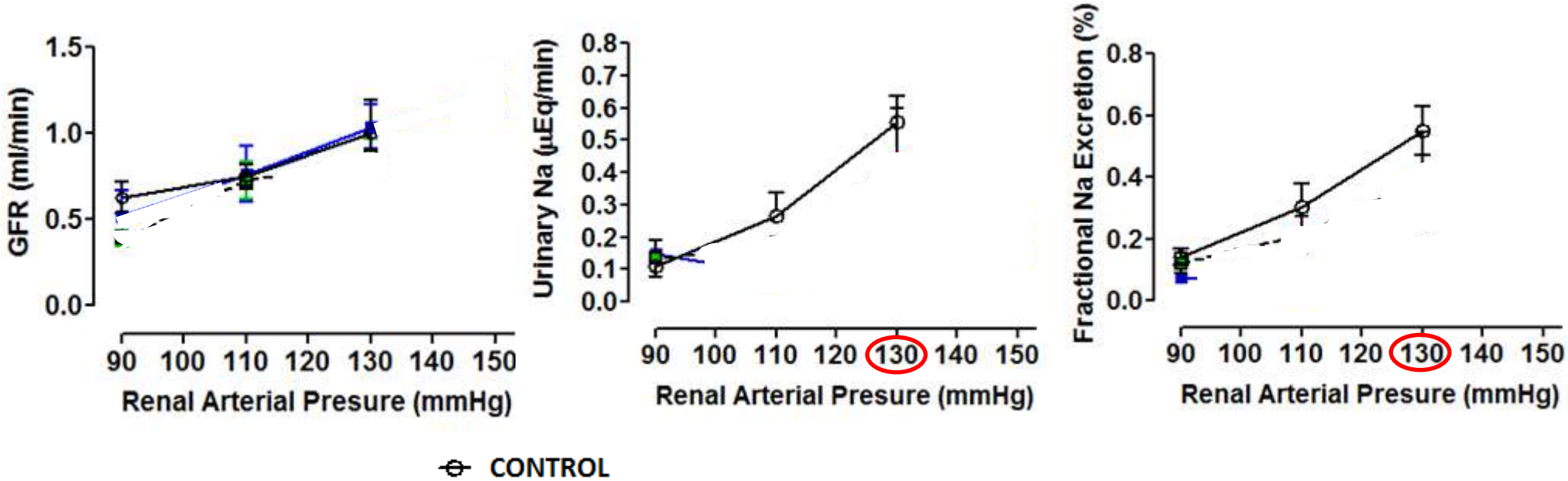
Guyton AC. Abnormal renal function and autoregulation in essential hypertension. Hypertension 1991; 18 (Suppl 5): 11149-53

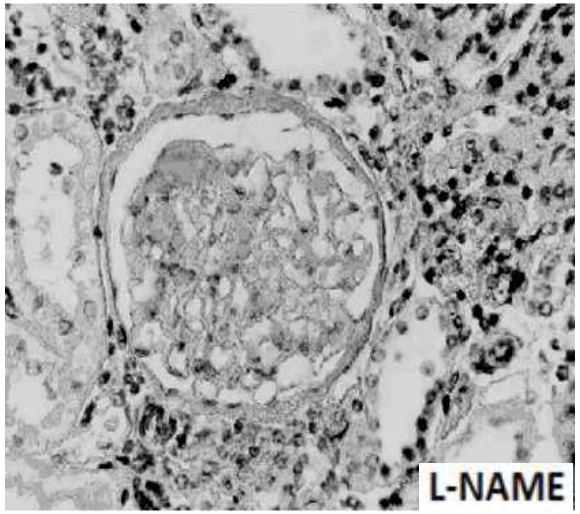
Arthur Guyton: Hypertension is Due to a Physiological Defect in Sodium Excretion

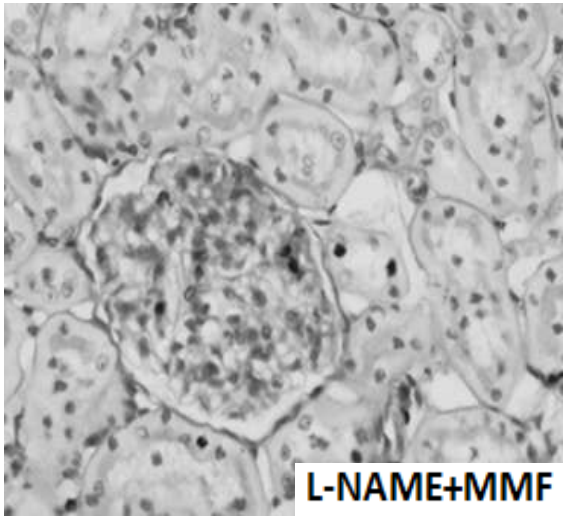


Guyton AC, et al Am J Med 1972; 52:584-594

Renal inflamación impairs pressure natriuresis (i)



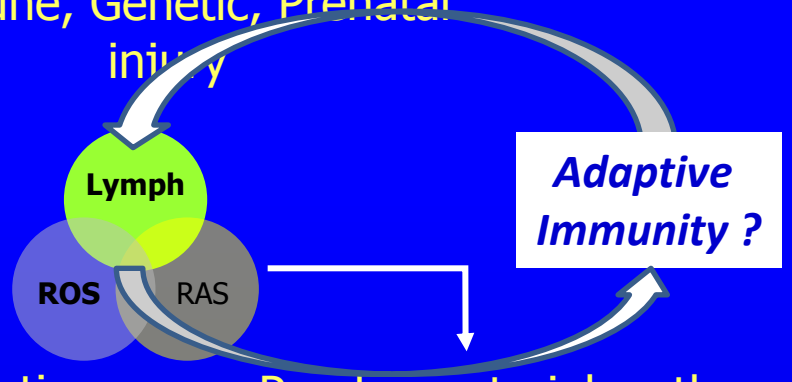




Clin Exp Physiol Pharmacol 2011

Initiation phase,
Normal kidney
Normal Na handling

Hemodynamic, Nephrotoxic, Metabolic ,
Immune, Genetic, Prenatal
injury



Subtle renal injury

TI ischemia → inflammation

↑ *vasoconstric, ↓ vasodilators*

Preglom arteriolopath
(SMC proliferation)

–RVR, ↓RBF, ↓ SNGFR,

↑Proximal Na reab
↓ Pressure natriuresis

↓ Filtered Na

Impaired Na
excretion

Na retention

Hypertension

Increased BP

Hypertensive kidney
Normal Na handling

Shift in pressure
natriuresis

↑ Perfusion pressure
Across arterial lesion

(Modified from NEJM, 2002)

Invited Review

Am J Physiol Renal Physiol 286: F606–F616, 2004;
10.1152/ajprenal.00269.2003.

Oxidative stress, renal infiltration of immune cells, and salt-sensitive hypertension: all for one and one for all

Bernardo Rodríguez-Iturbe,[1] Nosratola D. Vaziri,[2] Jaime Herrera-Acosta,[3] and Richard J. Johnson[4]

OXIDATIVE STRESS

↓

HSP

↓

Autoimmune Reactivity??

⇩

INTERSTITIAL IMMUNE INFILTRATION

Research studies in collaboration with

Jaime Herrera-Acosta *(Instituto Nacional de Cadiología, Mexico DF)*
Richard J. Johnson *(University of Colorado, Denver, Colorado)*
Nosratola D. Vaziri *(University of California, Irvine)*

Nephrology Laboratory, University Hospital and
Instituto Venezolano de Investigaciones Científicas (IVIC)-Zulia
2004-2011

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