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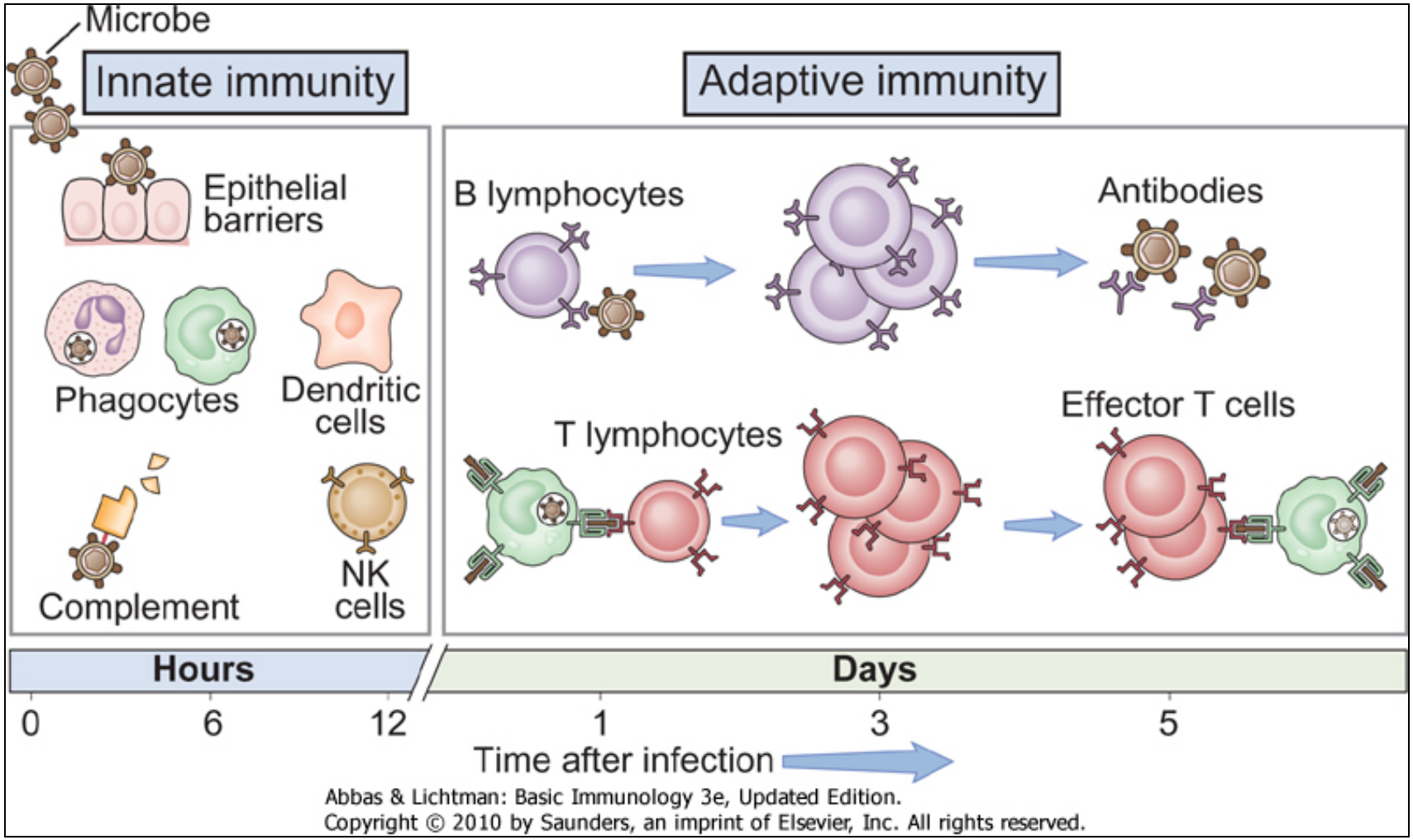
Cardiovascular Pathophysiology & Therapeutics

Novel therapeutic strategies to hypertension and translational approach to the cardiovascular diseases

Giuseppe Lembo

28.09.2015

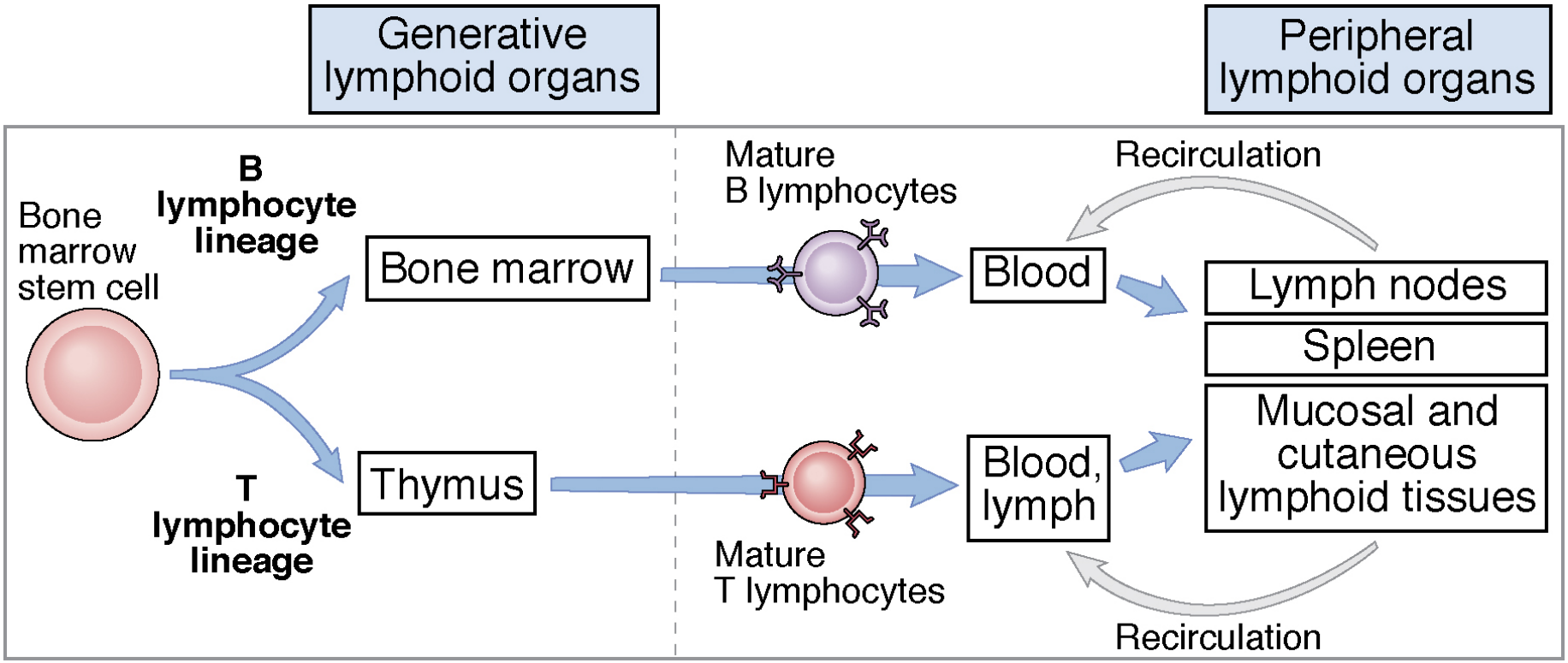
Innate and adaptive immunity



Innate immunity: always present (ready to attack)

Adaptive immunity: stimulated by exposure to microbe; more potent

Development of B and T lymphocytes



Congenital immunodeficiency diseases are often caused by blocks at different stages of lymphocyte maturation

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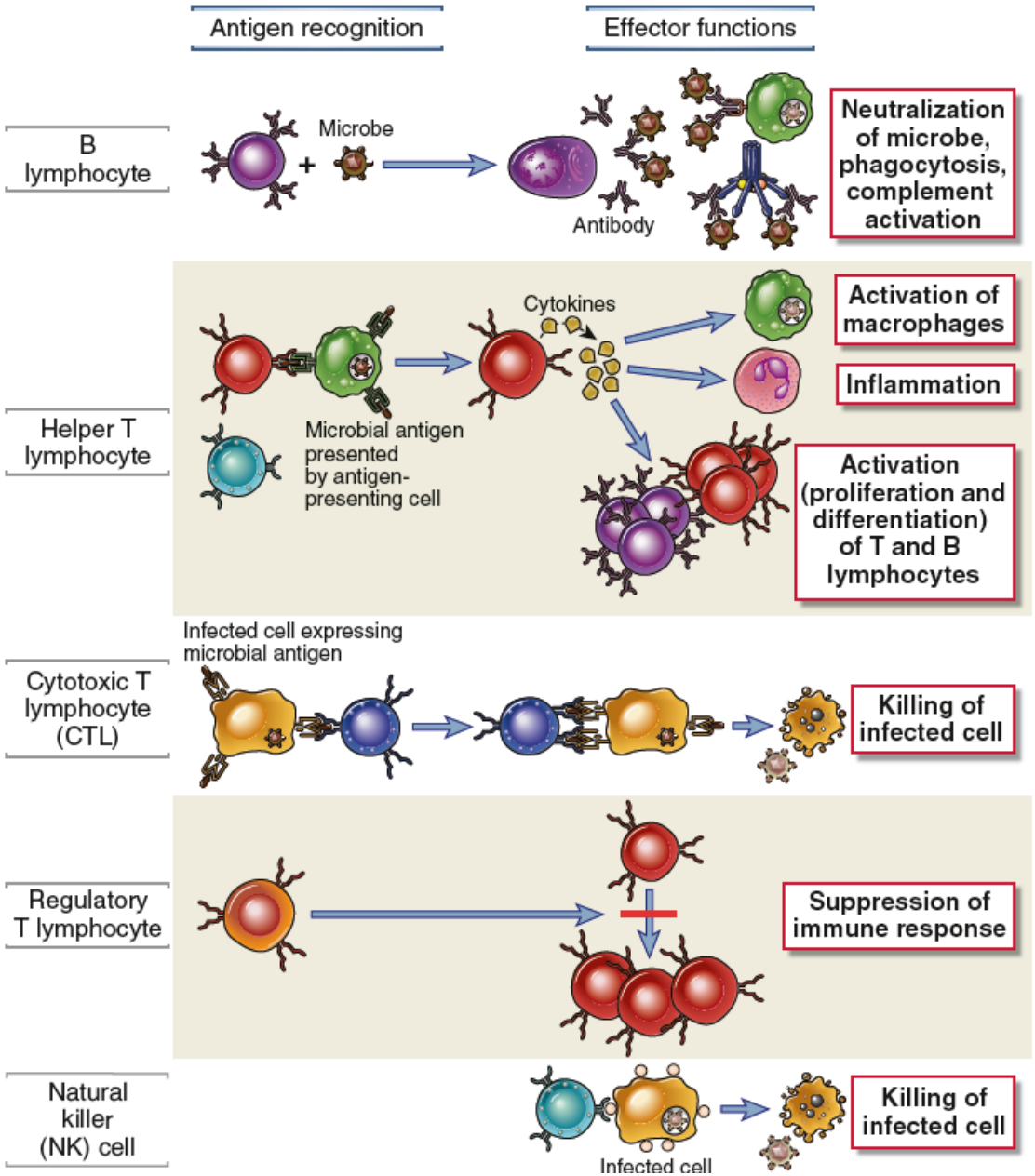
Classes of lymphocytes



Abbas, Lichtman and Pillai. *Cellular and Molecular Immunology, 7th edition, 2011*

Very early evidence of an involvement of immunity in hypertension

25. Evidence for an initial, **thymus** independent and a chronic, **thymus** dependent phase of DOCA and salt **hypertension** in **mice**.
Svendsen UG.
Acta Pathol Microbiol Scand A. 1976 Nov;84(6):523-8.
PMID: 998251
Similar articles

26. The role of **thymus** for the development and prognosis of **hypertension** and hypertensive vascular disease in **mice** following renal infarction.
Svendsen UG.
Acta Pathol Microbiol Scand A. 1976 May;84(3):235-43.
PMID: 1274588
Similar articles

27. The importance of **thymus** on the degree of increased blood pressure and vascular disease in **mice** with DOCA and salt **hypertension**.
Svendsen UG.
Acta Med Scand Suppl. 1976;602:19-21. No abstract available.
PMID: 1071943
Similar articles

28. Studies elucidating the importance of **thymus** on the degree of increased blood pressure and vascular disease in renal hypertensive **mice**. A comparison of the disease in nude and haired littermates.
Svendsen UG.
Acta Pathol Microbiol Scand A. 1975 Sep;83(5):568-72.
PMID: 126633
Similar articles

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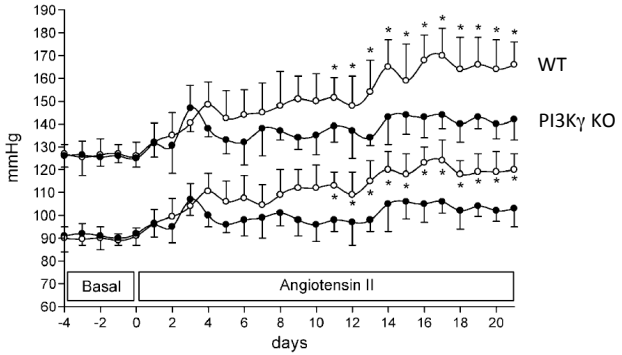
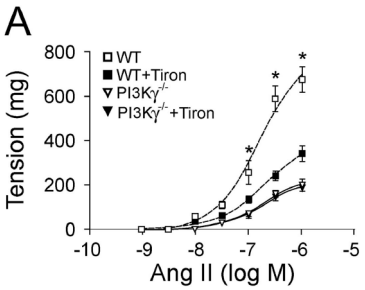
Vascular inflammation in Hypertension

Published April 11, 2005
JEM
ARTICL

Protection from angiotensin II–mediated vasculotoxic and hypertensive response in mice lacking PI3Kγ

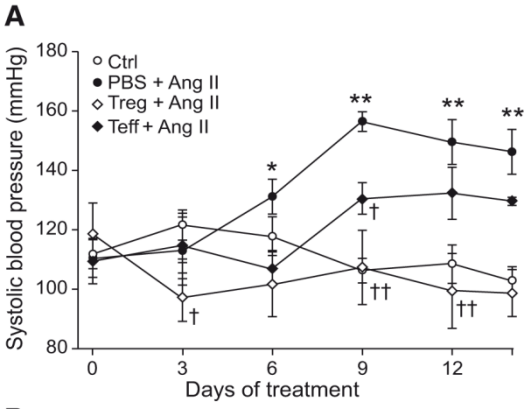
Carmine Vecchione,[1] Enrico Patrucco,[2] Gennaro Marino,[1] Laura Barberis, Roberta Poulet,[1] Alessandra Aretini,[1] Angelo Maffei,[1] Maria Teresa Gentile Marianna Storto,[1] Ornella Azzolino,[2] Mara Brancaccio,[2] Gian Luca Colussi Umberto Bettarini,[1] Fiorella Altruda,[2] Lorenzo Silengo,[2] Guido Tarone,[2] Mathias P. Wymann,[3] Emilio Hirsch,[2] and Giuseppe Lembo[1,4]

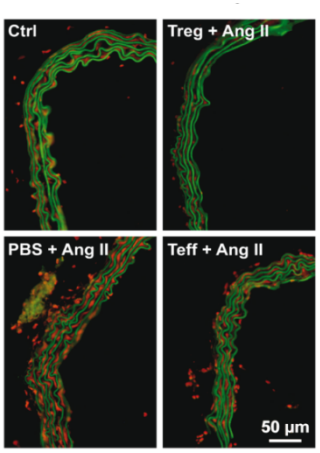




T Regulatory Lymphocytes Prevent Angiotensin II–Induced Hypertension and Vascular Injury

Tlili Barhoumi, Daniel A. Kasal, Melissa W. Li, Layla Shbat, Pascal Laurant, Mario F. Neves, Pierre Paradis, Ernesto L. Schiffrin





Barhoumi et al. Hypertension. 2011 Mar;57(3):469-76.

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Available online at www.sciencedirect.com

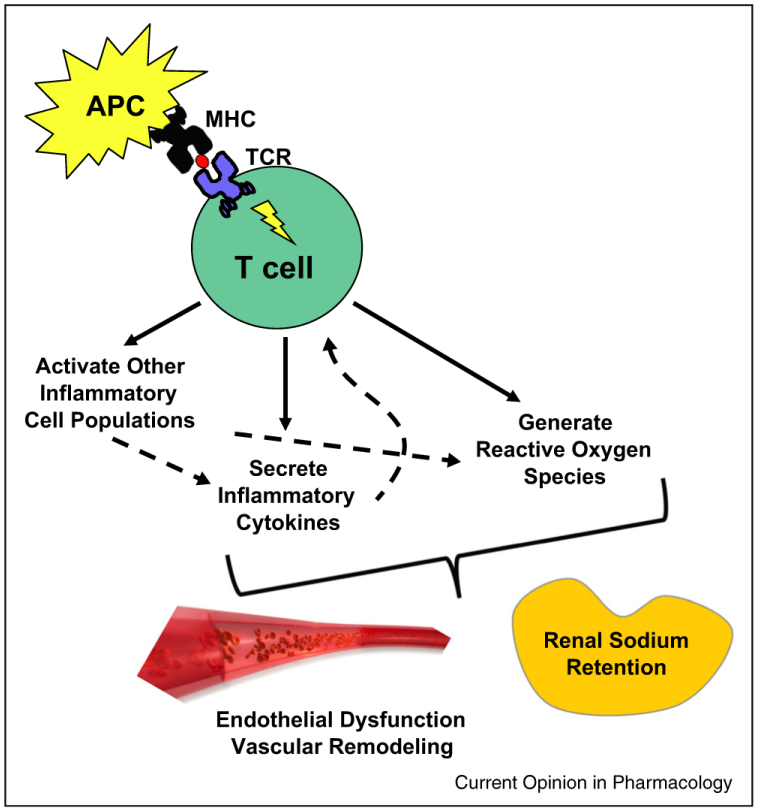
ScienceDirect

ELSEVIER

Current Opinion in Pharmacology

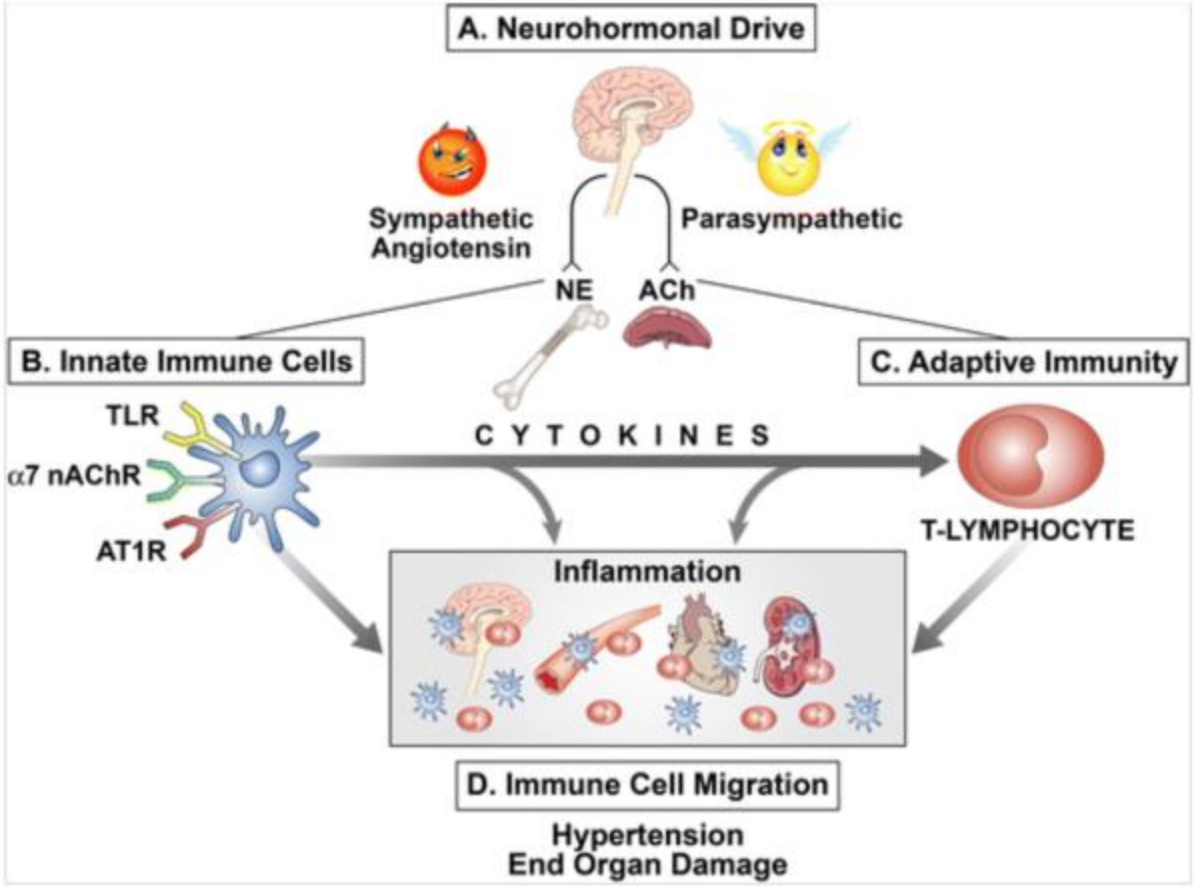
Role of T lymphocytes in hypertension

Jiandong Zhang and Steven D Crowley



Zhang J, Crowley SD. Curr Opin Pharmacol. 2015 Apr;21:14-9.

Dual role of immune system in hypertension? «organ damage» and «etiology»



Singh et al. Immunologic Research 2014, 59: 1;243-253

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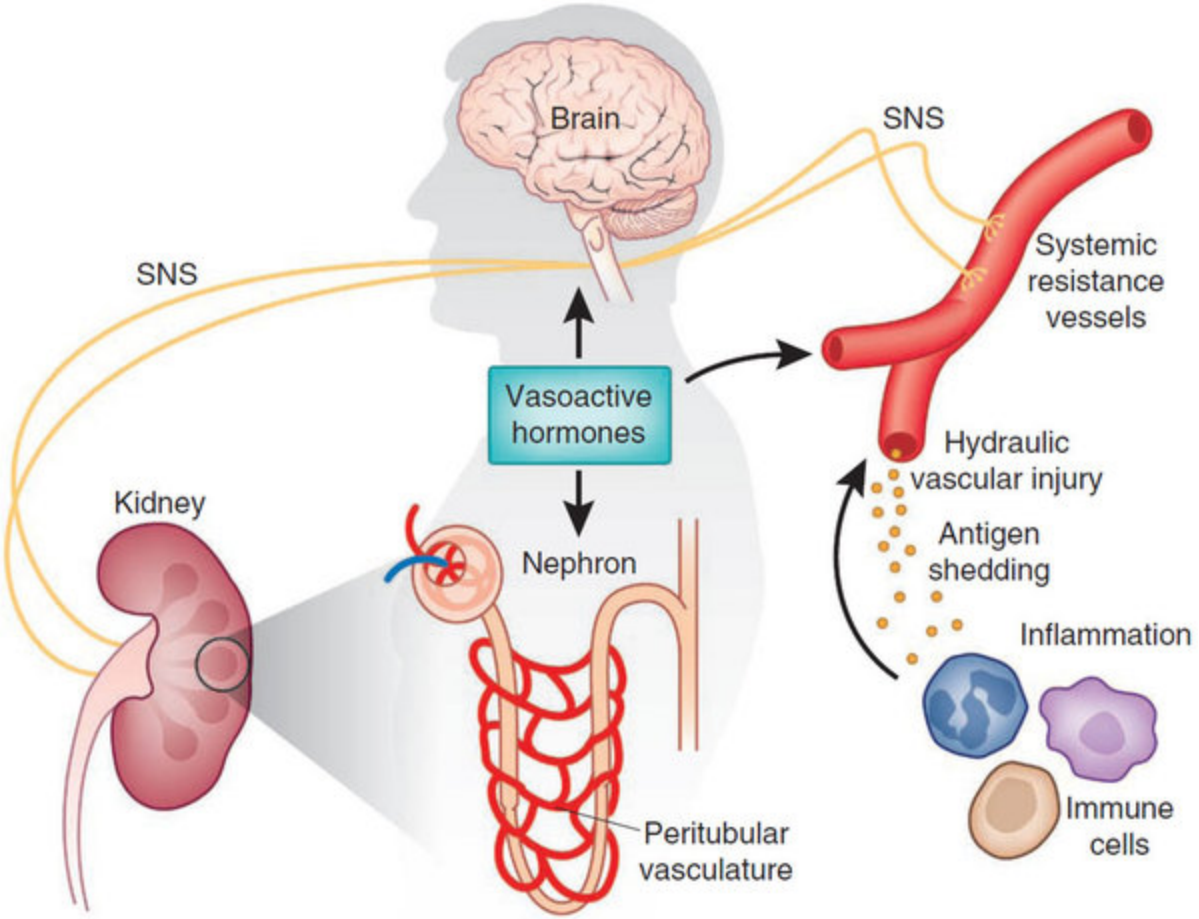
Under pressure:
the search for the essential mechanisms of hypertension



Coffman, Nature Medicine 2011; 17, 1402–1409.

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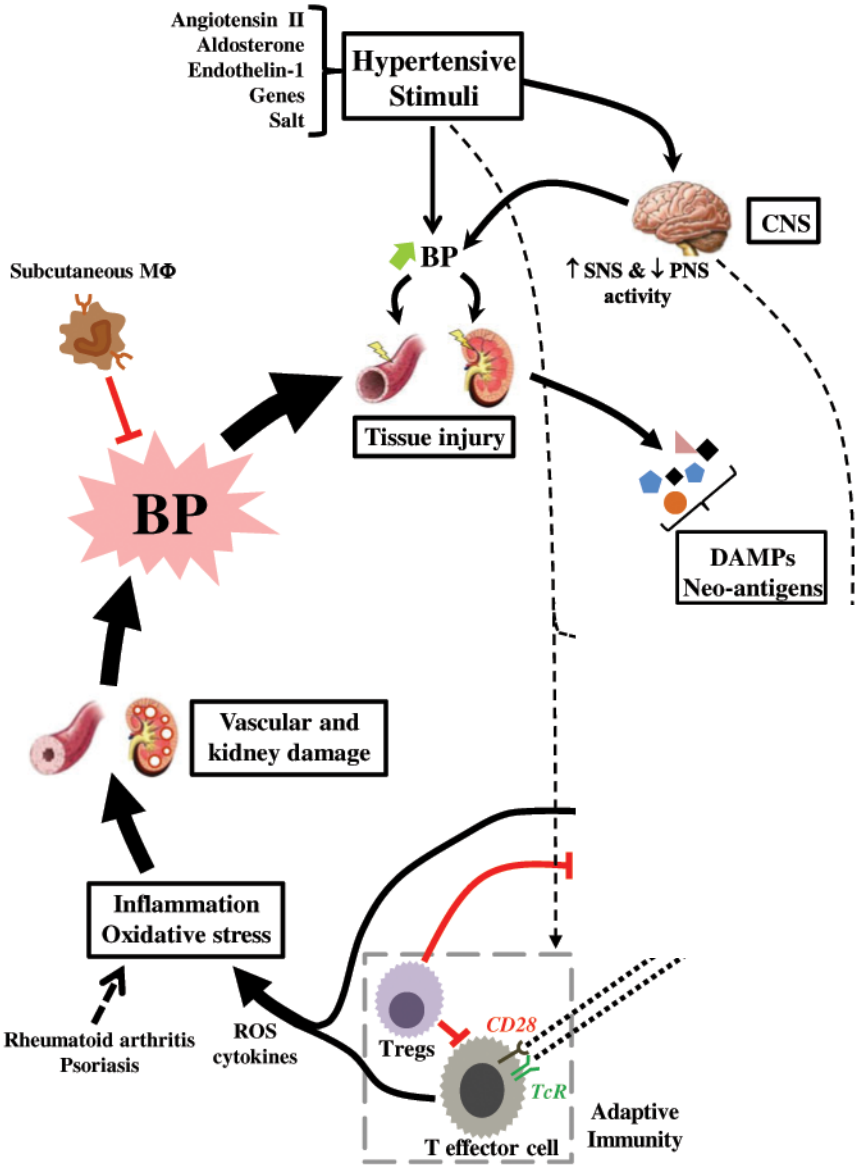
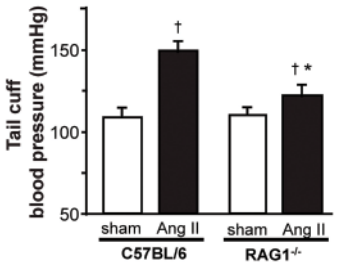
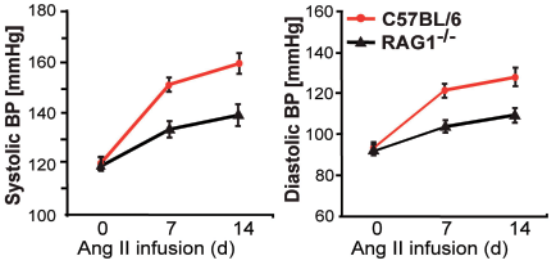
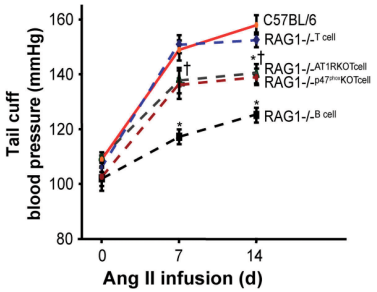
Role of T lymphocytes in Hypertension



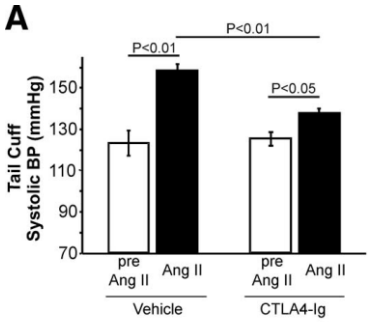
Mian et al., Curr Hypertens Rep 2014



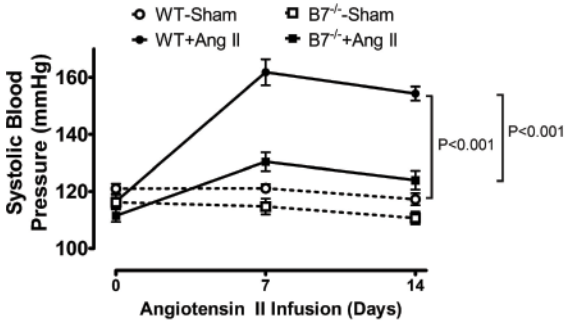




Guzik et al., J Exp Med 2007



Vihn et al., Circulation 2010

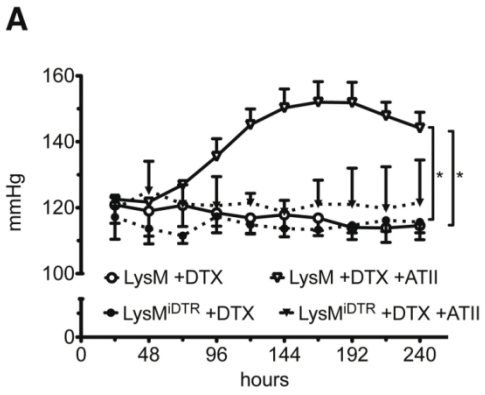


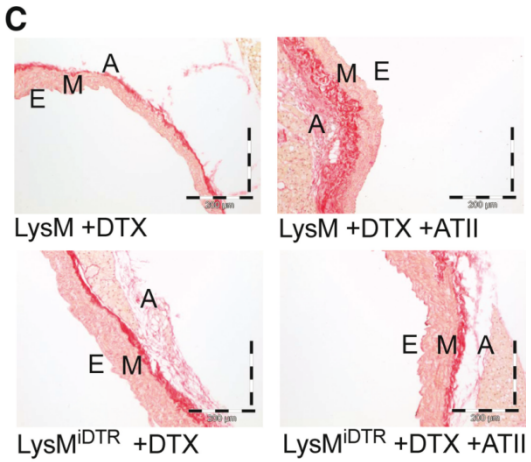
Vascular Medicine

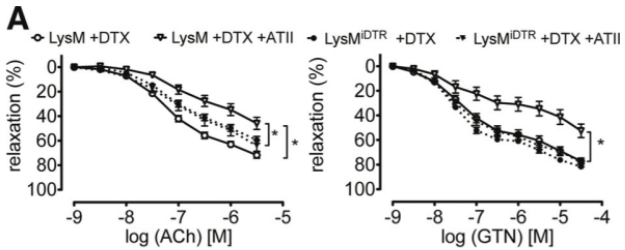
Lysozyme M–Positive Monocytes Mediate Angiotensin II–Induced Arterial Hypertension and Vascular Dysfunction

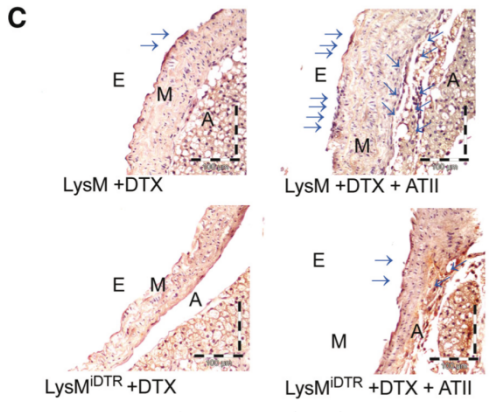
Philip Wenzel, MD*; Maike Knorr, MD*; Sabine Kossmann, MSc; Jan Stratmann, BSc; Michael Hausding, PhD; Swenja Schuhmacher, PhD; Susanne H. Karbach, MD; Melanie Schwenk, MSc; Nir Yogev, PhD; Eberhard Schulz, MD; Matthias Oelze, PhD; Stephan Grabbe, MD; Helmut Jonuleit, PhD; Christian Becker, PhD; Andreas Daiber, PhD; Ari Waisman, PhD; Thomas Münzel, MD

Circulation. 2011;124:1370-1381.









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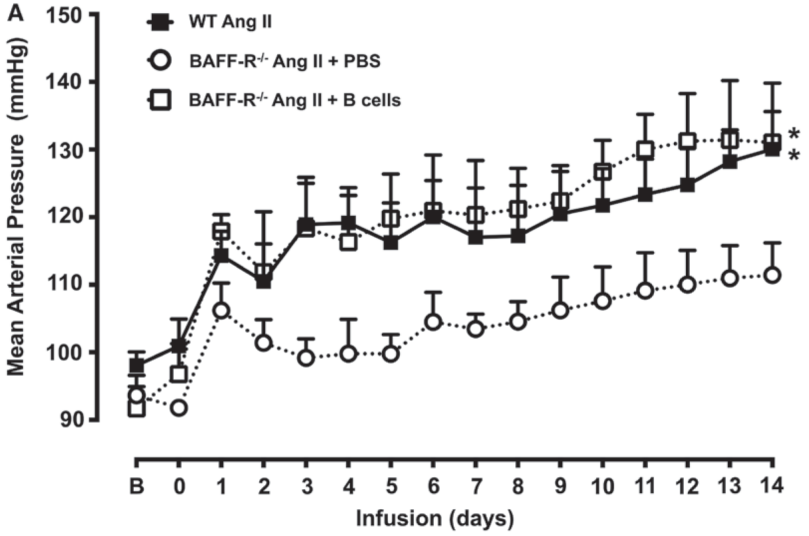
B cells in hypertension

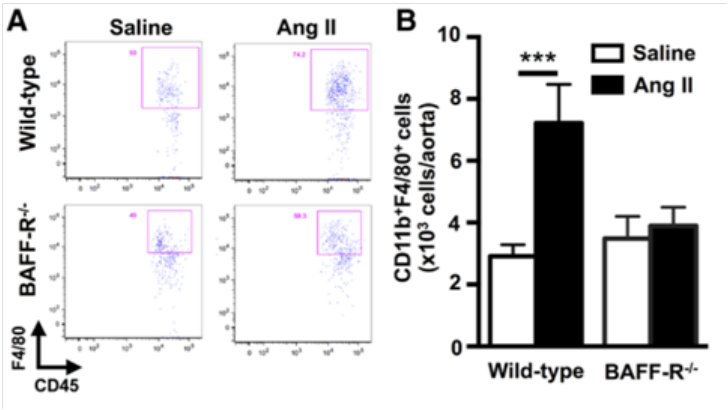
Original Article

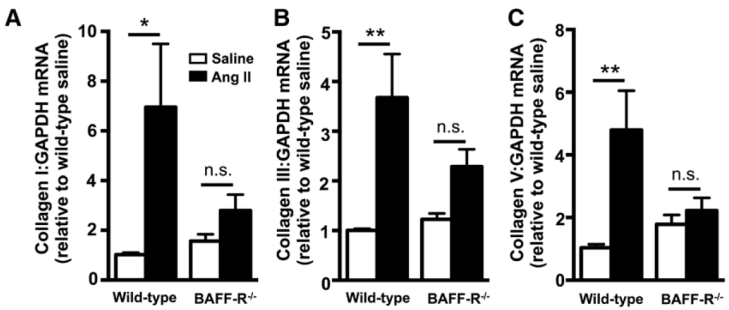
Obligatory Role for B Cells in the Development of Angiotensin II–Dependent Hypertension

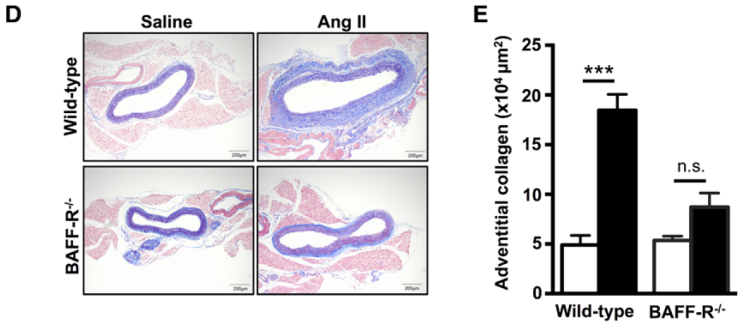
Christopher T. Chan, Christopher G. Sobey, Maggie Lieu, Dorota Ferens, Michelle M. Kett, Henry Diep, Hyun Ah Kim, Shalini M. Krishnan, Caitlin V. Lewis, Ekaterina Salimova, Peter Tipping, Antony Vinh, Chrishan S. Samuel, Karlheinz Peter, Tomasz J. Guzik, Tin S. Kyaw, Ban-Hock Toh, Alexander Bobik, Grant R. Drummond

Hypertension. 2015;66:00-00. DOI: 10.1161/HYPERTENSIONAHA.115.05779









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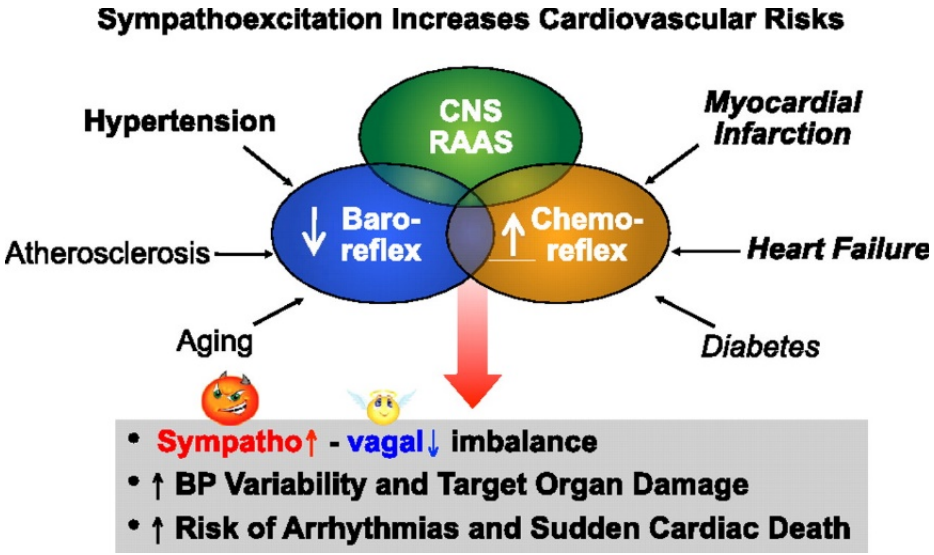
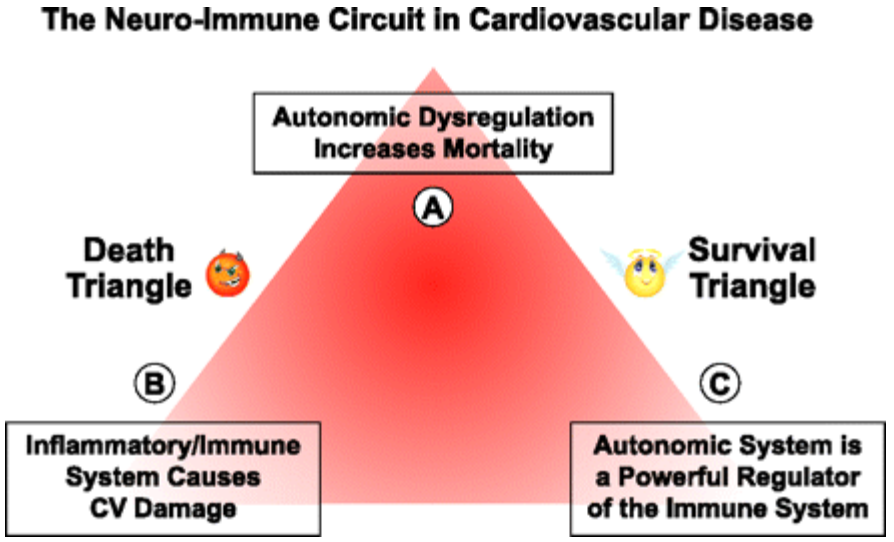
Neuro-immune Dealing in Hypertension





Singh et al. Immunologic Research 2014, 59: 1;243-253

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Renal Denervation After SYMPLICITY HTN-3: Where Do We Go?

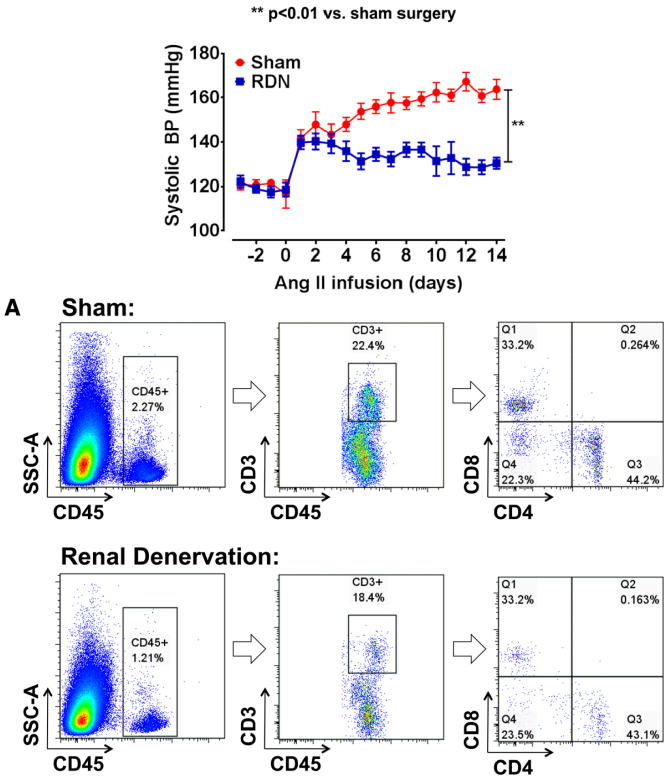
The NEW ENGLAND JOURNAL of MEDICINE

Integrative Physiology

Renal Denervation Prevents Immune Cell Activation and Renal Inflammation in Angiotensin II–Induced Hypertension

Liang Xiao, Annet Kirabo, Jing Wu, Mohamed A. Saleh, Linjue Zhu, Feng Wang, Takamune Takahashi, Roxana Loperena, Jason D. Foss, Raymond L. Mernaugh, Wei Chen, Jackson Roberts II, John W. Osborn, Hana A. Itani, David G. Harrison

Circ Res. 2015;117:547-557.

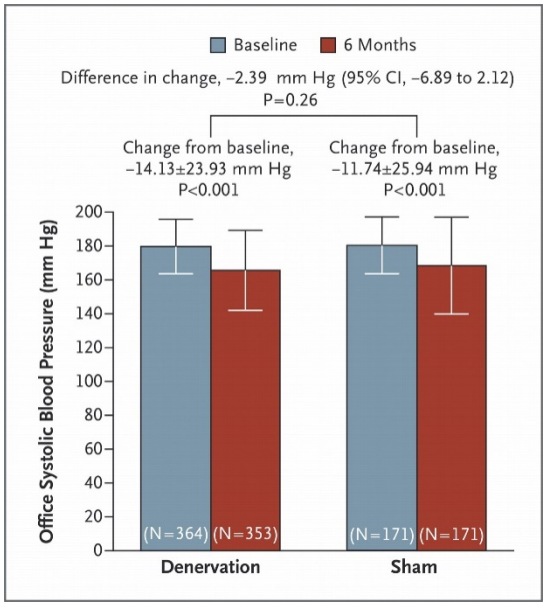


ORIGINAL ARTICLE

A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D., Ralph D'Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D., Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D., Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D., Raymond R. Townsend, M.D., and George L. Bakris, M.D., for the SYMPLICITY HTN-3 Investigators*

Primary Efficacy End Point

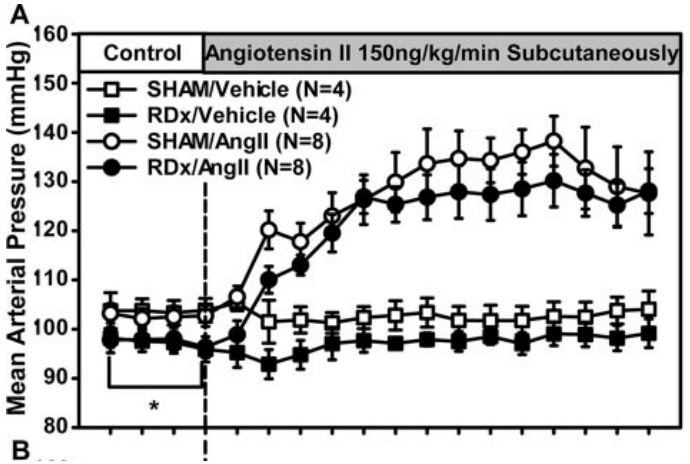


Bhatt DL et al. N Engl J Med 2014;370:1393-1401

HOW does AngII activate the immune system in the spleen?

DIRECT VS INDIRECT ACTIONS

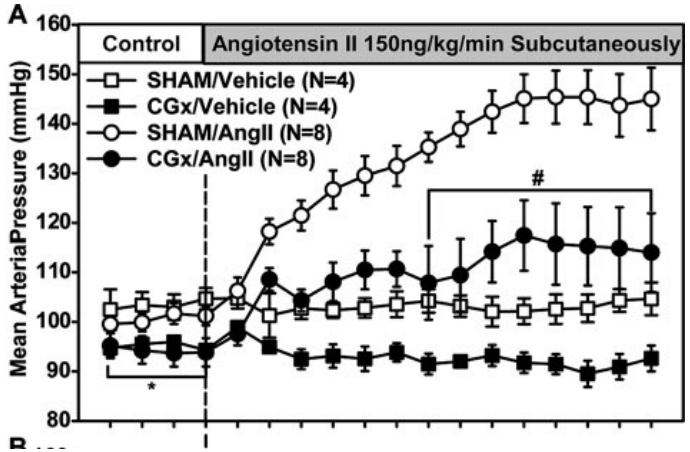
NA release from activated splanchnic sympathetic nerves is crucial for the development and maintenance of hypertension



The renal nerves have always gained attention in various experimental models of hypertension and in human hypertension

BUT

RDx does not attenuated AngII-induced hypertension



Celiac ganglionectomy (CGX) SIGNIFICANTLY ATTENUATES AngII-induced hypertension

King et al, Hypertension 2007

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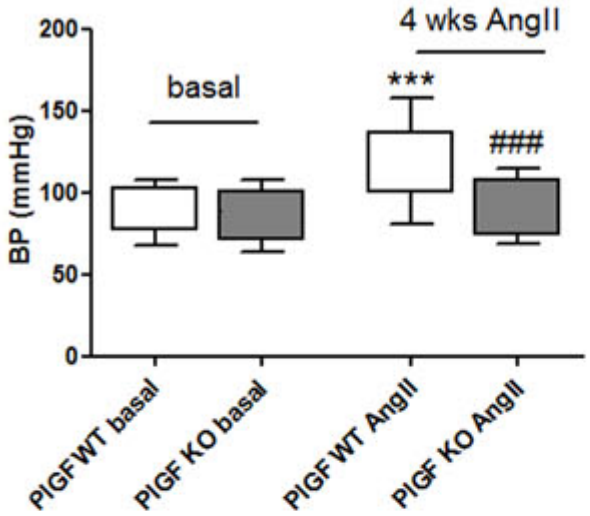
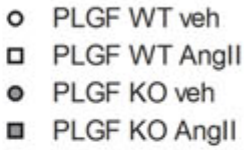
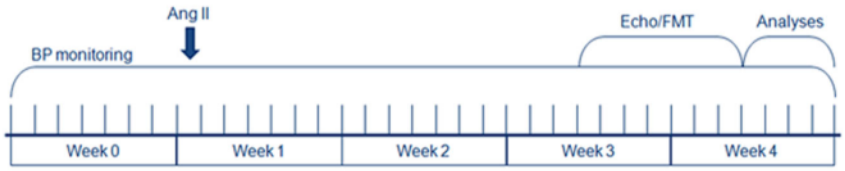
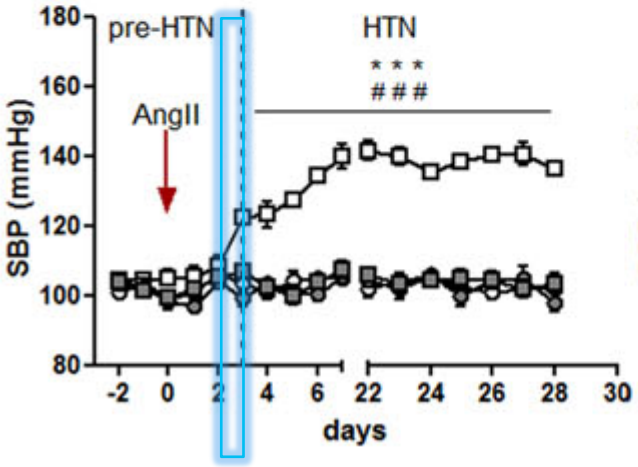
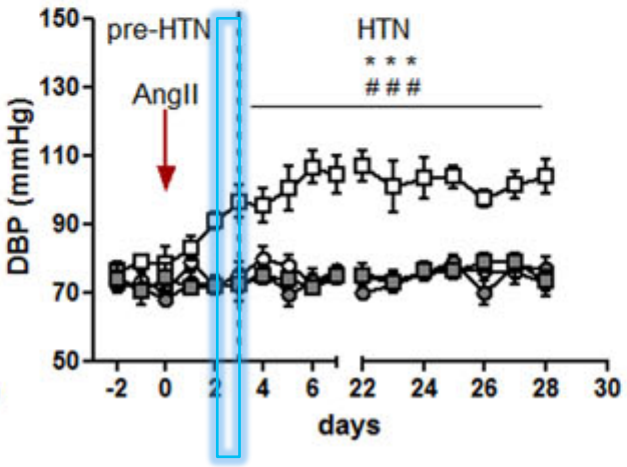
PLGF KO MICE ARE PROTECTED FROM ANGIOTENSIN II INDUCED HYPERTENSION

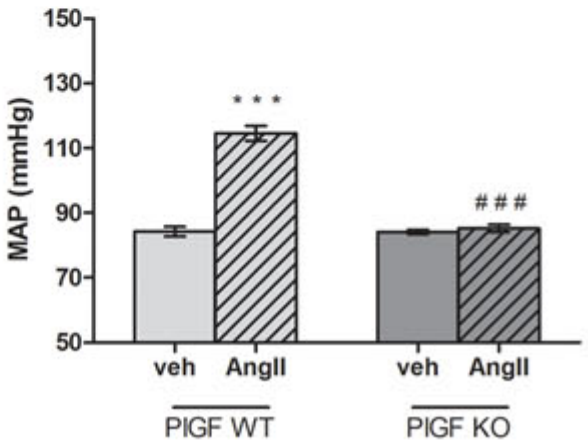












Carnevale et al., *Immunity 41, 737–752, November 20, 2014*

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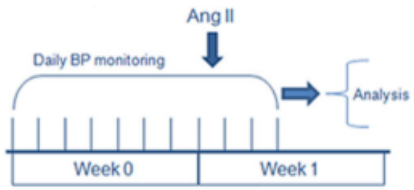
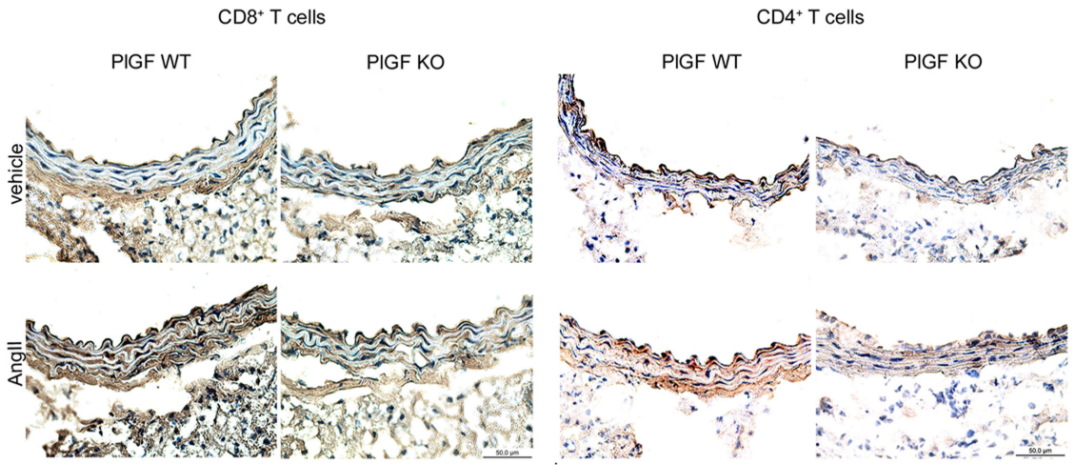
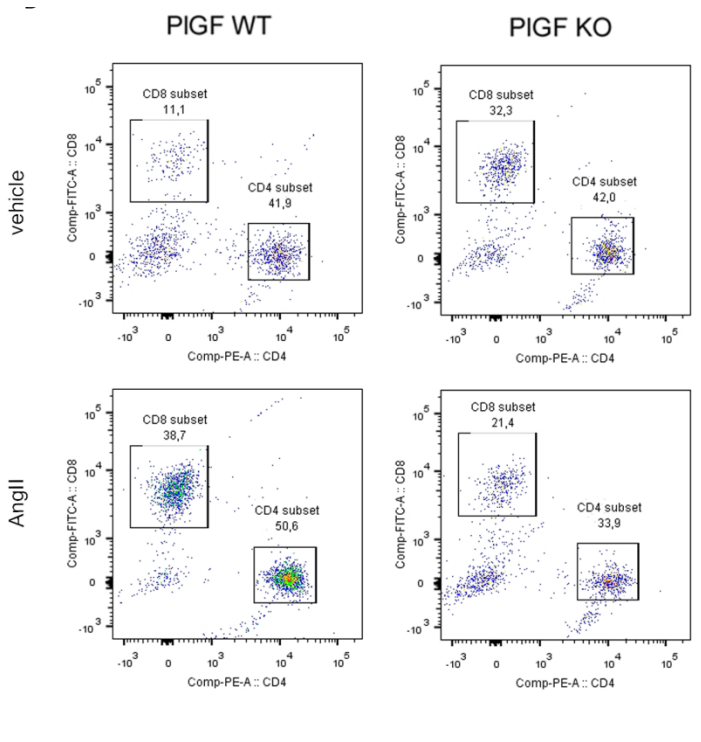
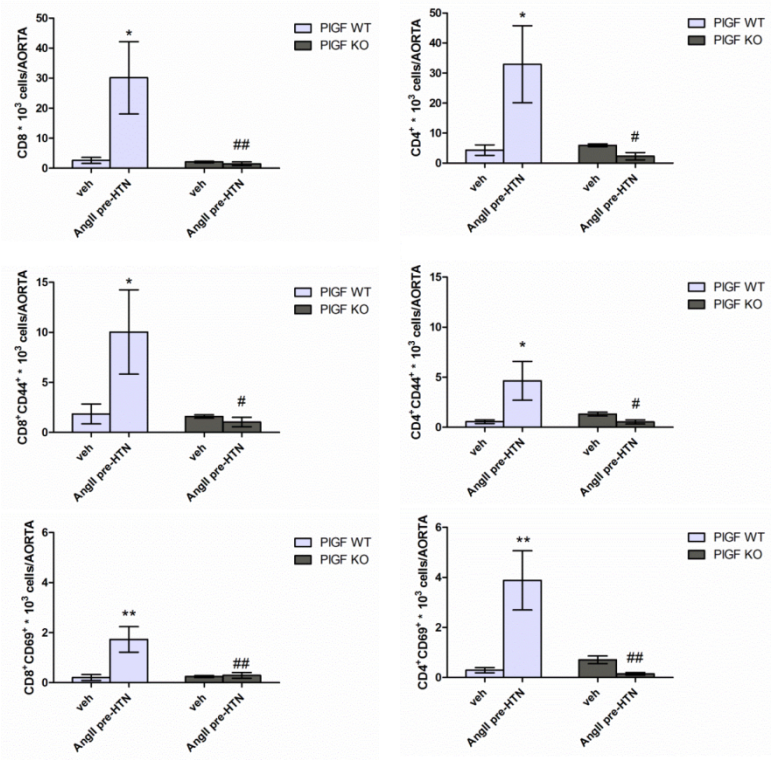
PLGF KO MICE ARE PROTECTED FROM EARLY ANGIOTENSIN II INDUCED T CELLS INFILTRATION IN TARGET ORGANS









Carnevale et al., *Immunity 41, 737–752, November 20, 2014*

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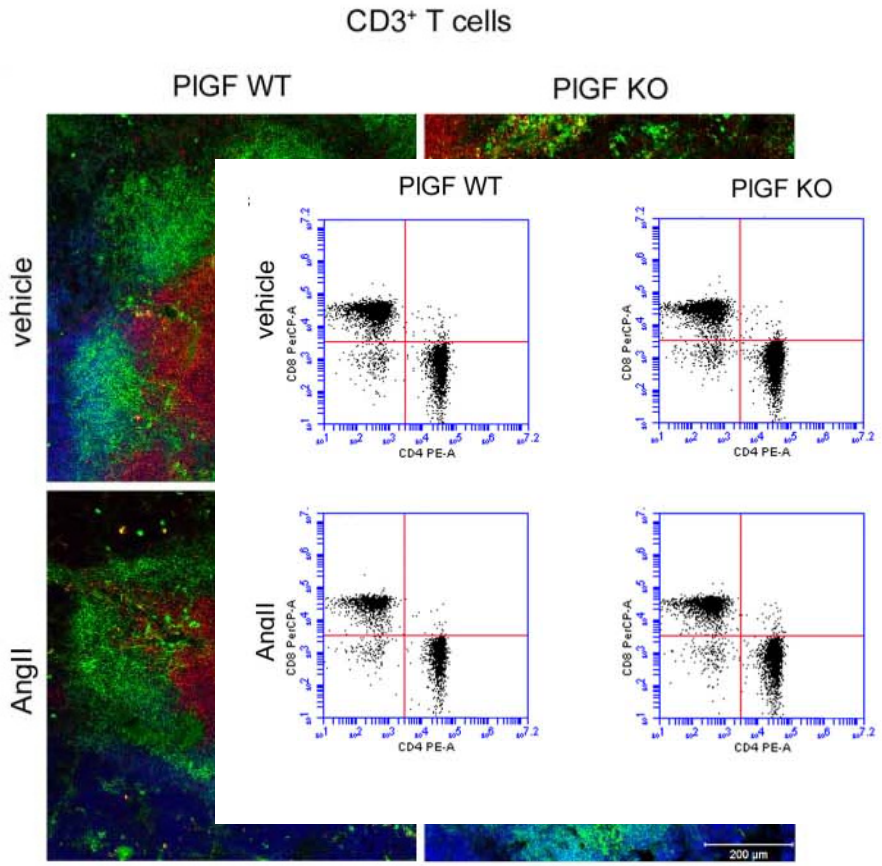
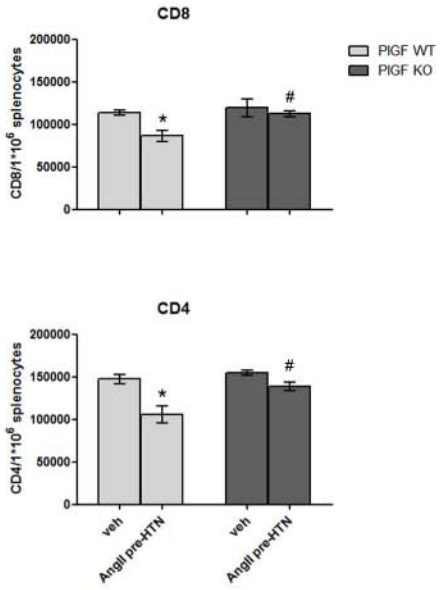
PLGF IS REQUIRED FOR SPLENIC T CELL EGRESSION UNDER HYPERTENSIVE CONDITIONS





Carnevale et al., *Immunity 41, 737–752, November 20, 2014*

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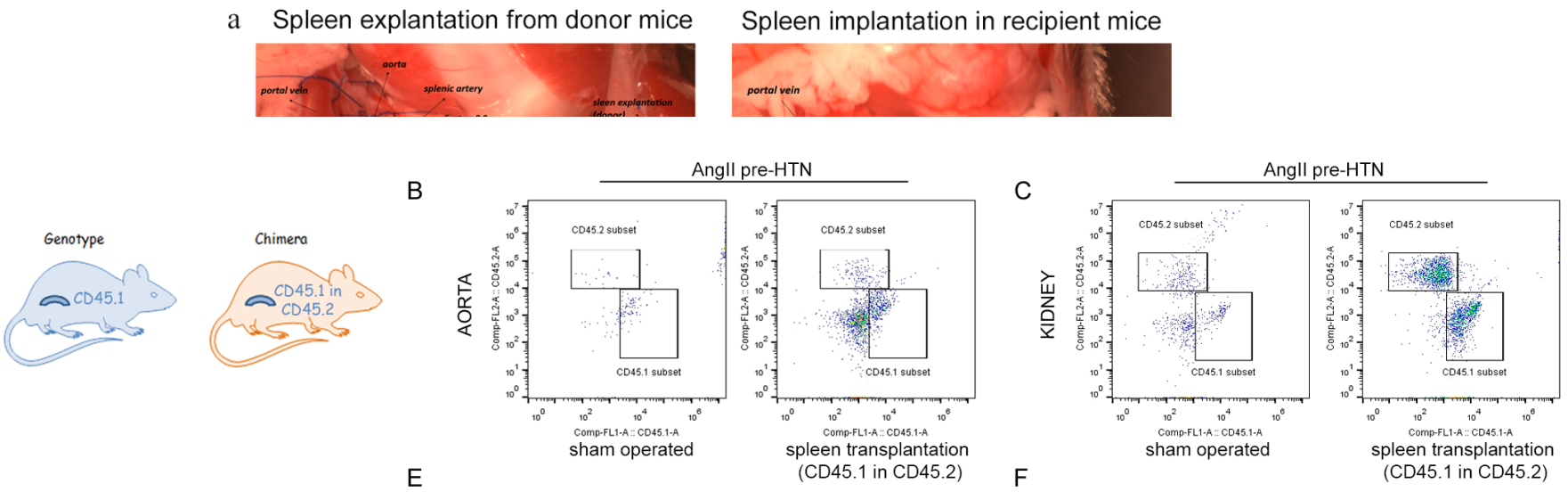
GENERATION OF CHIMERIC MICE BY SPLEEN TRANSPLANTATION

HELPS TO ELUCIDATE THE SELECTIVE CONTRIBUTION OF THE SPLEEN IN HYPERTENSION



Carnevale et al., *Immunity 41, 737–752, November 20, 2014*

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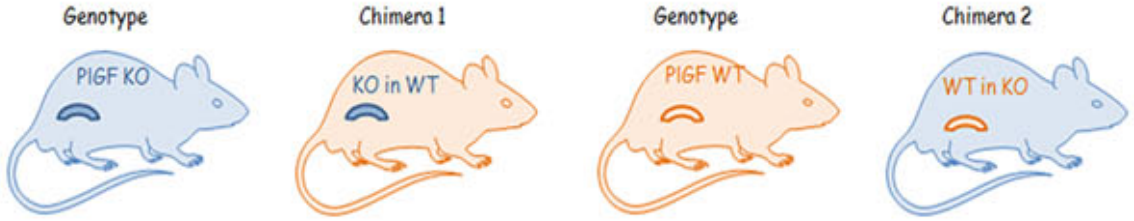
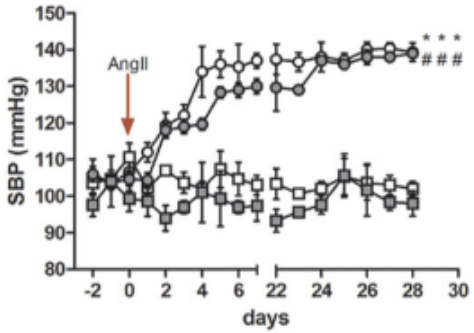
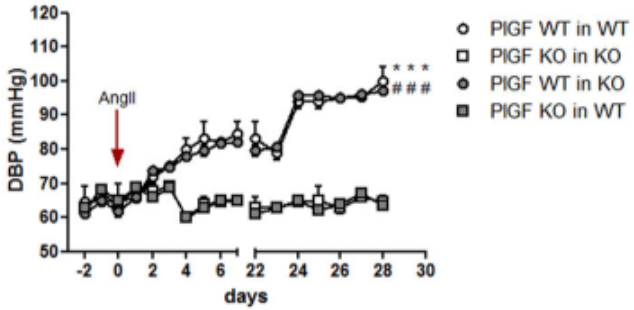
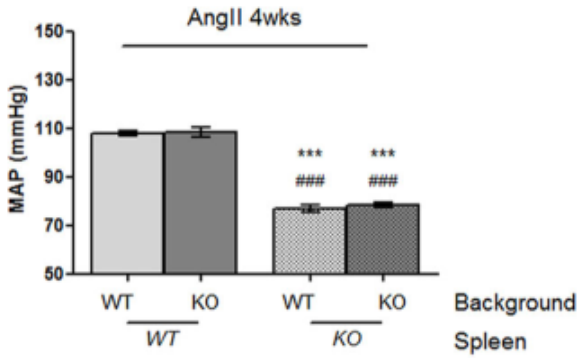
GENERATION OF CHIMERIC MICE BY SPLEEN TRANSPLANTATION

HELPS TO ELUCIDATE THE SELECTIVE CONTRIBUTION OF PLGF IN THE SPLEEN









Carnevale et al., *Immunity 41, 737–752, November 20, 2014*

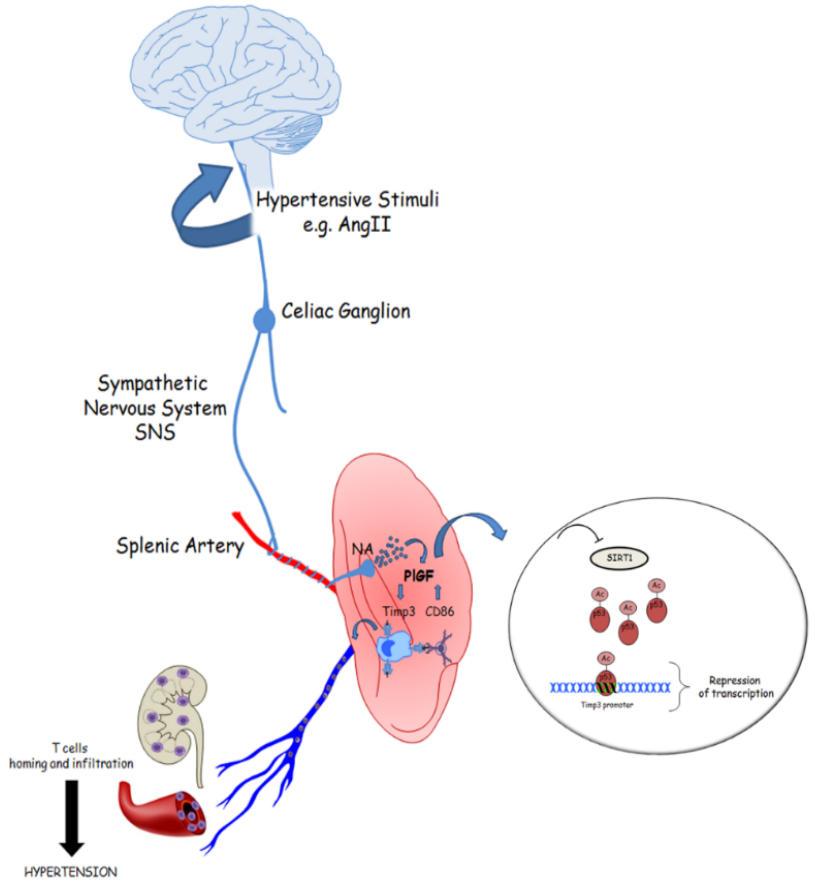
CardioPaTh

Immunity
Article

The Angiogenic Factor PlGF Mediates a Neuroimmune Interaction in the Spleen to Allow the Onset of Hypertension

Daniela Carnevale,[1,2] Fabio Pallante,[1] Valentina Fardella,[1] Stefania Fardella,[1] Roberta Iacobucci,[1] Massimo Federici,[3] Giuseppe Cifelli,[1] Massimiliano De Lucia,[1] and Giuseppe Lembo[1,2,*]

Immunity *41*, 737–752, November 20, 2014 ©2014 Elsevier Inc.



Immunity
Previews

Hypertension: An Immune Disorder?

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http://dx.doi.org/10.1016/j.immuni.2014.11.007

T cell depletion can prevent hypertension in experimental animals. What is the nature of T cell activation in hypertension? In this issue of *Immunity*, Carnevale et al. (2014) implicate PlGF signaling in a reservoir of splenic T cells.

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