



"Farmacologia Cardiovascular"



Tecido Adiposo Perivascular (PVAT)

Eliana H. Akamine
eliakamine@usp.br
2020

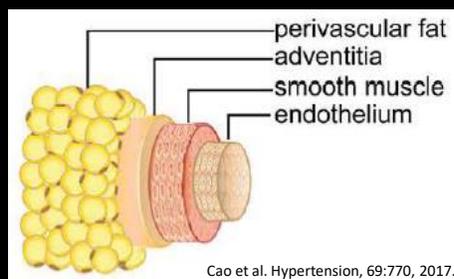
Tópicos

- 1) Características gerais do PVAT
- 2) Adipocinas e mediadores secretados pelo PVAT
- 3) PVAT e regulação do tônus vascular

TECIDO ADIPOSEO PERIVASCULAR

Definição

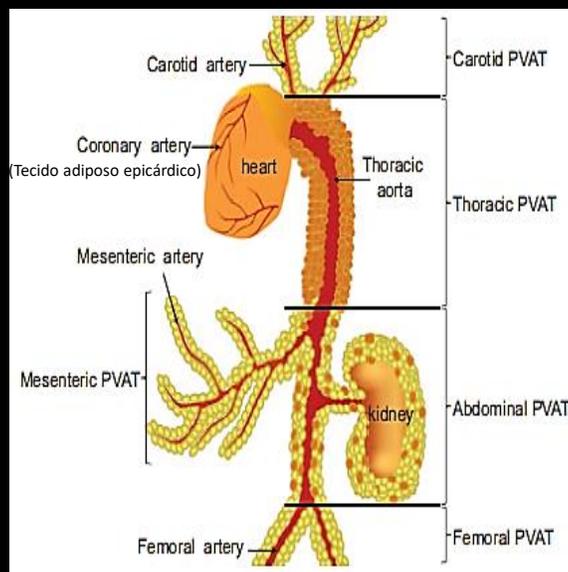
Tecido adiposo que circunda os vasos sanguíneos.



TECIDO ADIPOSEO PERIVASCULAR

Localização

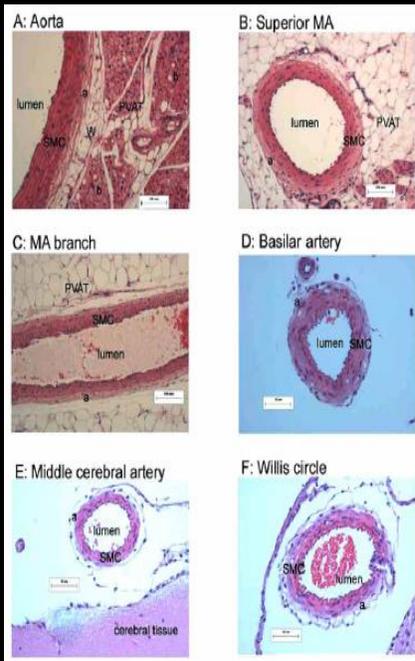
- diâmetro > 50-100 μm



Brown et al. Atheroscler Thromb Vasc Biol, 34:1621, 2014.

TECIDO ADIPOSO PERIVASCULAR

Localização

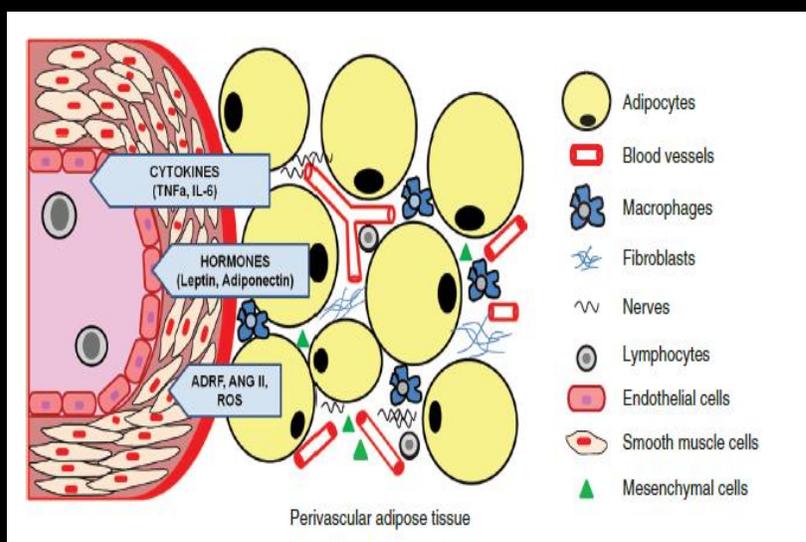


- exceção: vasos sanguíneos cerebrais

Gao YJ. Cur Pharmacol Des, 13:2185, 2007.

TECIDO ADIPOSO PERIVASCULAR

Composição

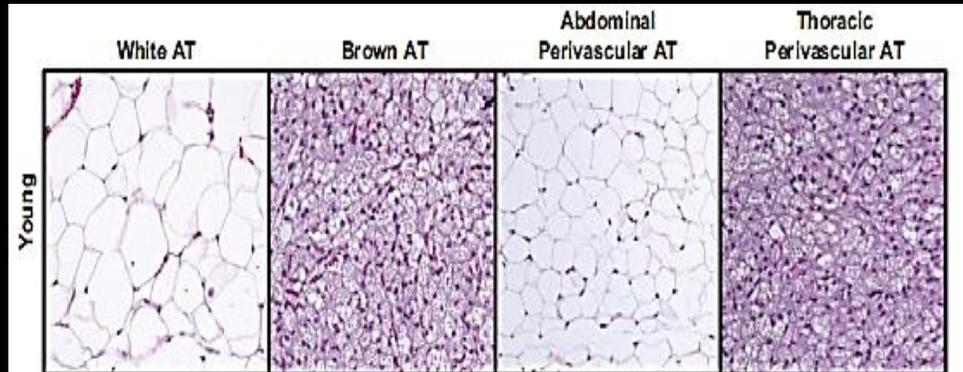


Even et al. Horm Mol Biol Clin Invest, 19:89, 2014.

TECIDO ADIPOSO PERIVASCULAR

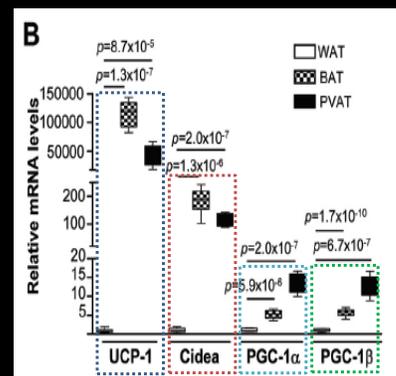
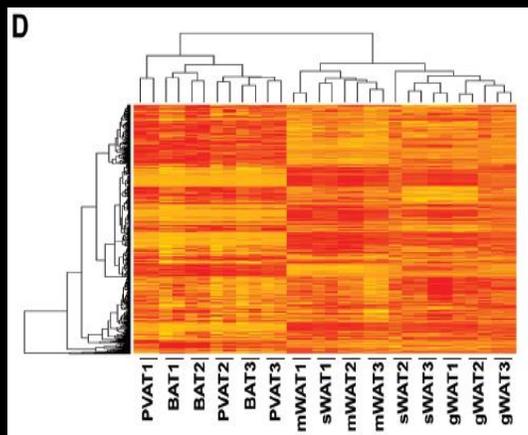
Diferenças regionais

PVAT da aorta torácica é semelhante ao BAT e da aorta abdominal é semelhante ao WAT



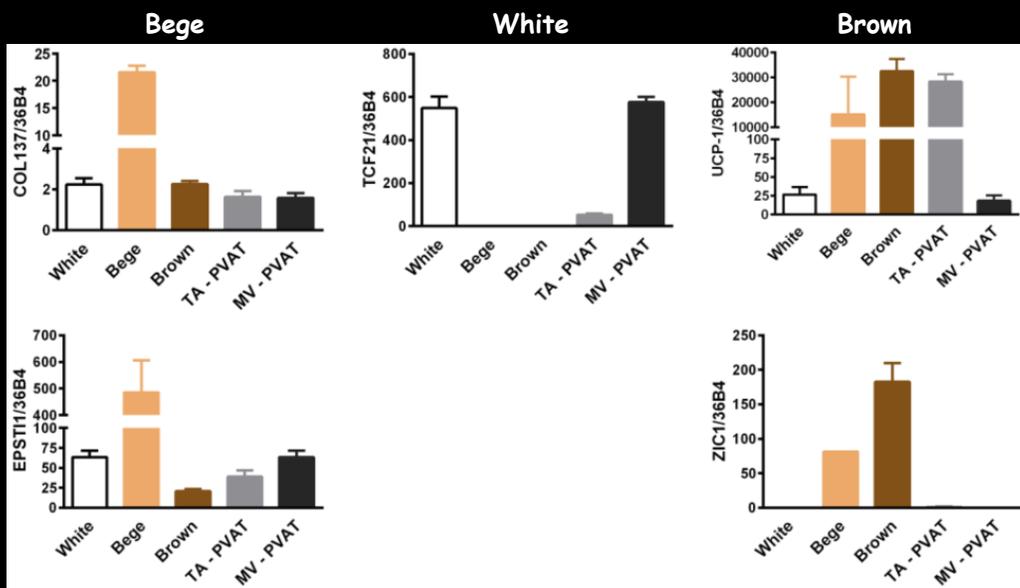
Padilla et al. Am J Physiol, 304:R543, 2013.

PVAT da aorta torácica é semelhante ao BAT



Chang et al. Circulation, 126:1067-1078, 2012.

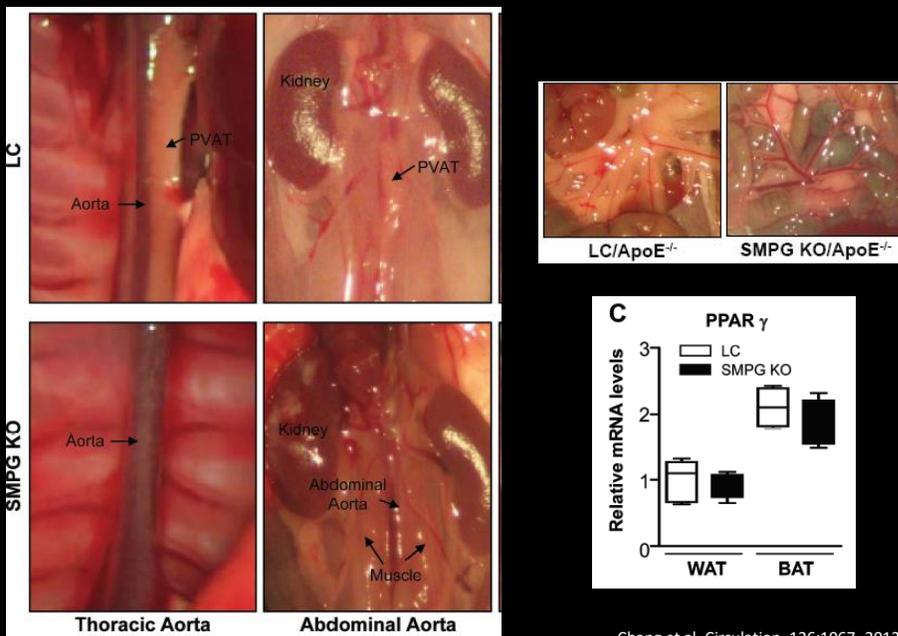
PVAT parece ser outro tipo de tecido adiposo



Hashimoto CM, unpublished data.

TECIDO ADIPOSO PERIVASCULAR

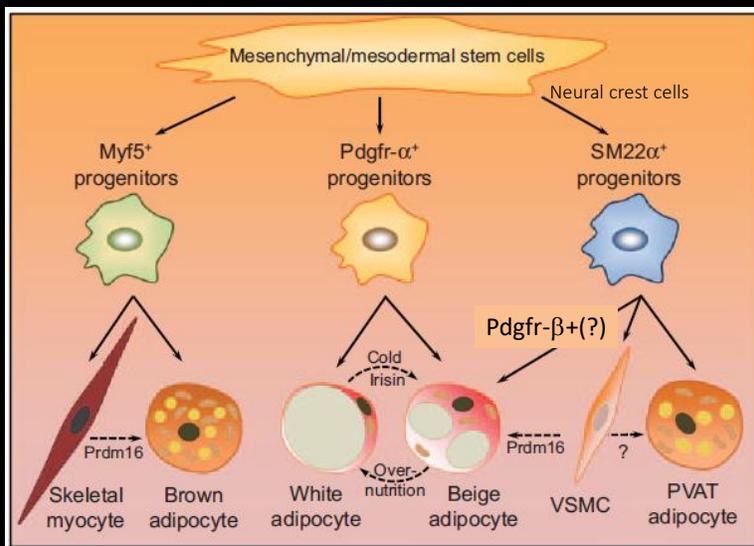
Origem



Chang et al. Circulation, 126:1067, 2012.

TECIDO ADIPOSEO PERIVASCULAR

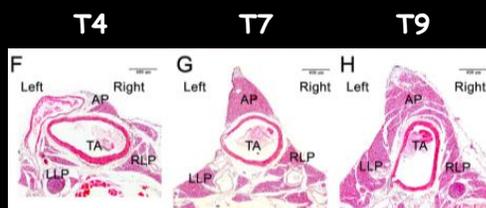
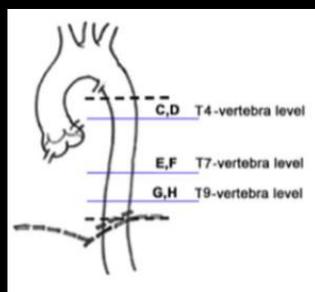
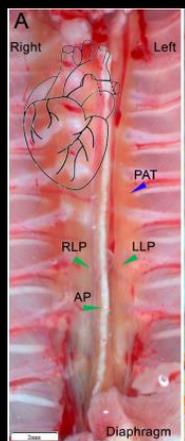
Origem



Para revisão: Brown et al. Atheroscler Thromb Vasc Biol, 34:1621, 2014; Hildebrand et al., Front Physiol, 9:70, doi: 10.3389/fphys.2018.00070
Fu et al. Atheroscler Thromb Vasc Biol, 39:1629, 2019

TECIDO ADIPOSEO PERIVASCULAR

Origem

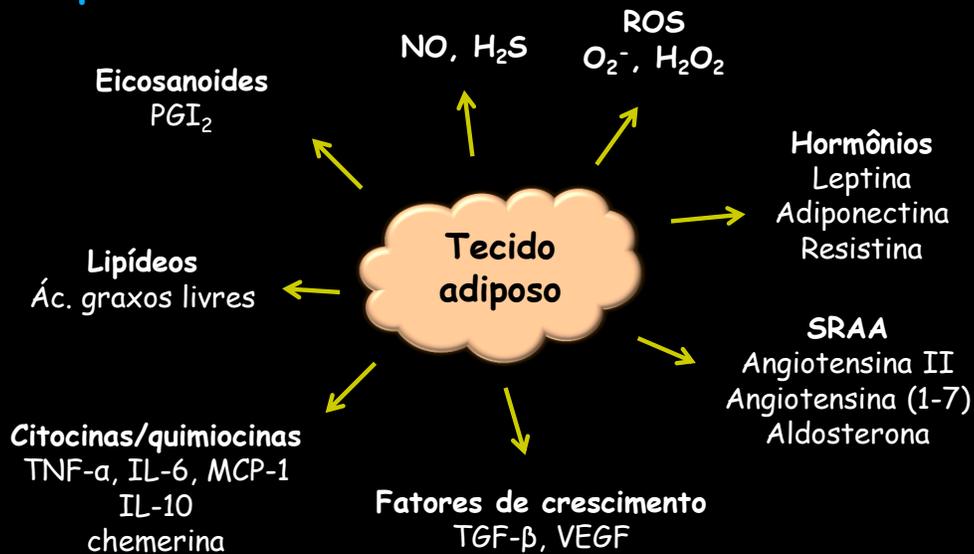


- 3 depósitos diferentes:
 - Cels. progenitoras
 - # adipócitos marrons UCP-1+
 - Transcriptoma
 - Regulação tônus vascular

Ye et al. Cell Mol Life Sci, 76:777, 2019.

TECIDO ADIPOSEO PERIVASCULAR

Adipocinas/Mediadores



Para revisão: Gollash, Ann Rev Pharmacol Toxicol, 57:14.1, 2017; Zaborska et al., Br J Pharmacol, 174:3388, 2017

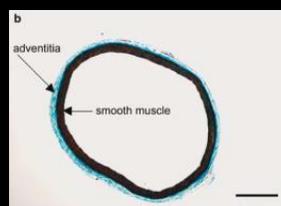
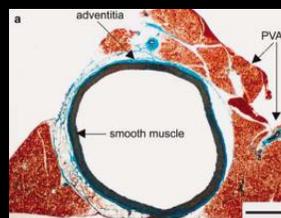
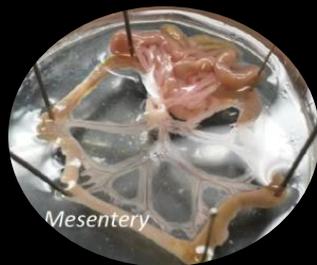
TECIDO ADIPOSEO PERIVASCULAR

Função

Regulação:

- tônus vascular
- proliferação e migração músculo liso
- temperatura intravascular

TECIDO ADIPOSITO PERIVASCULAR



Gao et al. Br J Pharmacol, 151:323, 2007.

Clin Exp Hypertens A, 1991;13(2):277-96.

Influence of perivascular adipose tissue on rat aortic smooth muscle responsiveness.

Soltis EE¹, Cassis LA.

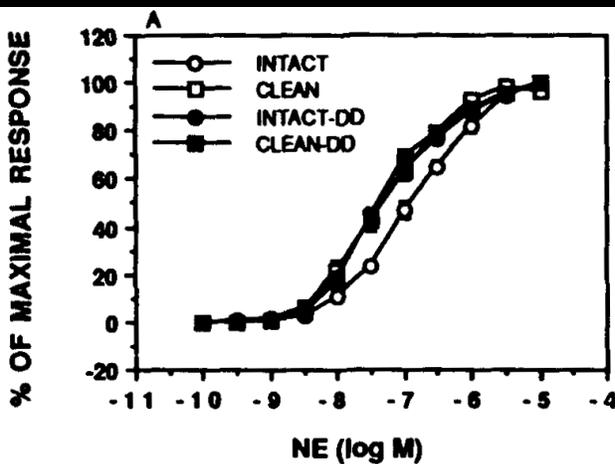
Aorta torácica
Rato Sprague-Dawley



PVAT-



PVAT+

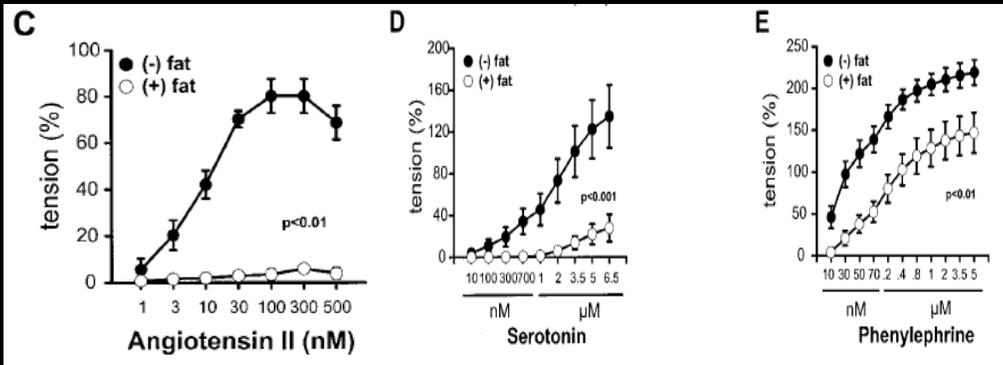


Periadventitial fat releases a vascular relaxing factor

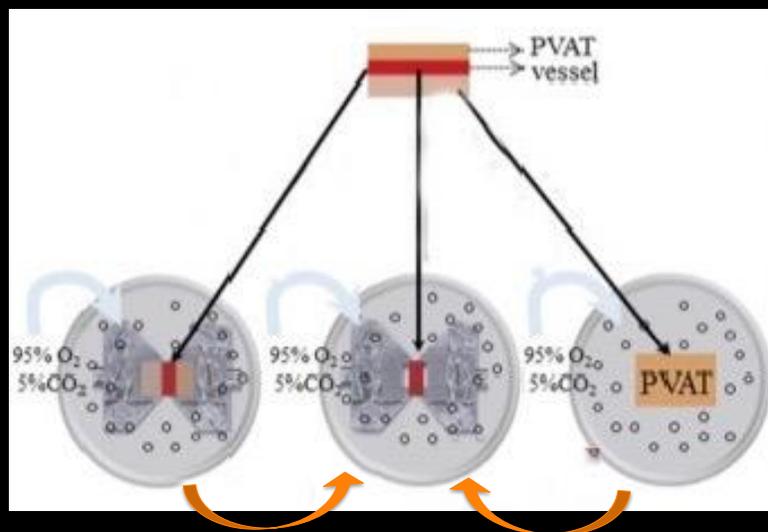
MATTHIAS LÖHN,¹ GALYNA DUBROVSKA,¹ BIRGIT LAUTERBACH,
FRIEDRICH C. LUFT, MAIK GOLLASCH, AND ARYA M. SHARMA²

HELIOS Klinikum Berlin, Franz Volhard Clinic and Max Delbrück Center for Molecular Medicine,
Medical Faculty of the Charité, Humboldt University of Berlin, Germany

Aorta torácica
Rato Sprague-Dawley



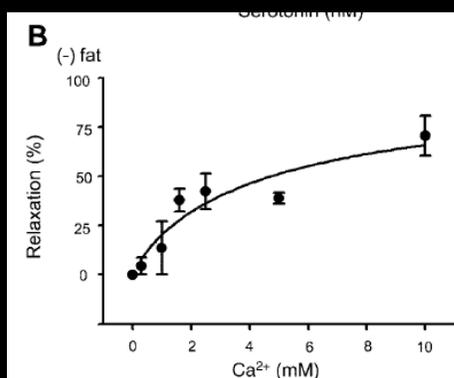
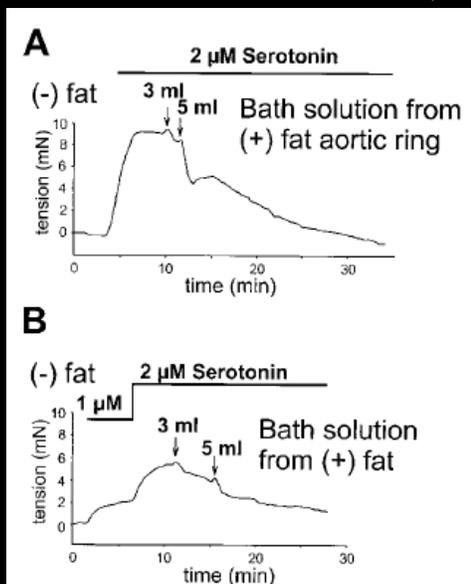
Löhn et al. FASEB J, 16:1057-1063, 2002.



Villacorta e Chang. Horm Mol Biol Clin Invest, 21:137-147, 2015.

Ação anticontrátil do PVAT: PDRF

Aorta torácica
Rato Sprague-Dawley



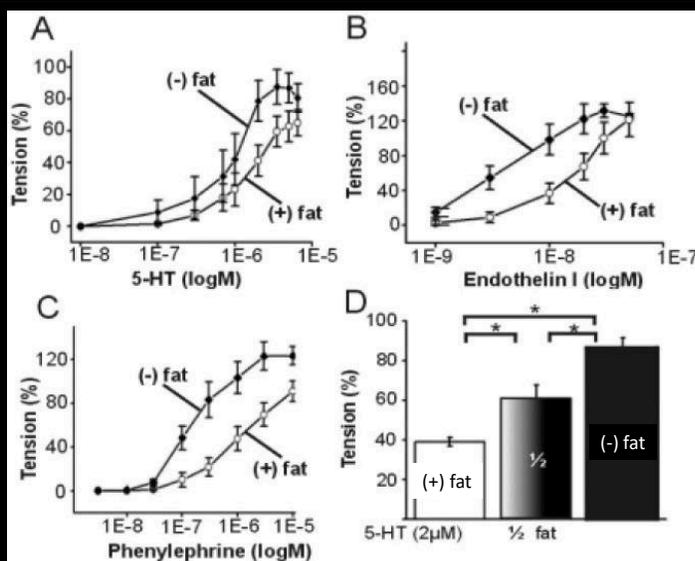
Löhn et al. FASEB J, 16:1057-1063, 2002.

Dubrovskaya et al. Am J Physiol, 286:H1107, 2004.

Visceral Periadventitial Adipose Tissue Regulates Arterial Tone of Mesenteric Arteries

Stefan Verlohren, Galyna Dubrovskaya, Suk-Ying Tsang, Kirill Essin, Friedrich C. Luft, Yu Huang, Maik Gollasch

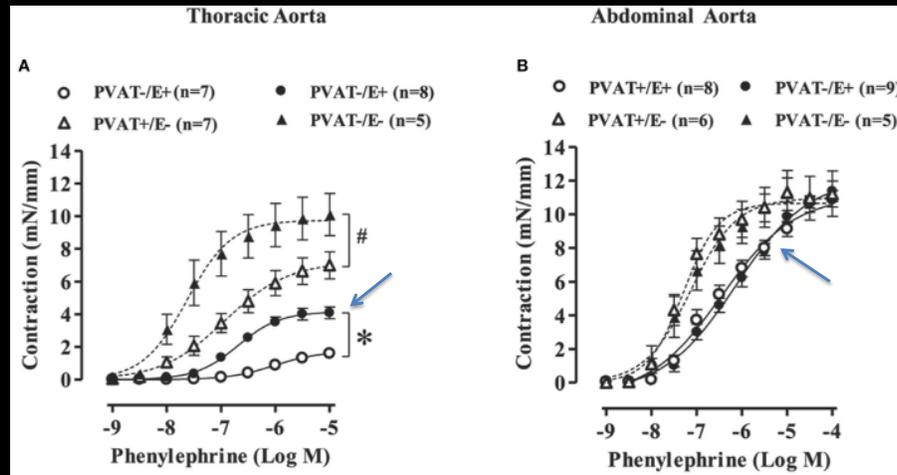
AMS
Rato Sprague-Dawley



Verlohren et al. Hypertension, 44:271-276, 2004.

Diferente ação anticontrátil do PVAT da aorta torácica e abdominal

Rato Wistar



Victorio, Fontes et al. Front Physiol, 7:295, 2016.

Ação anticontrátil do PVAT: PDRF

Tipo PVAT

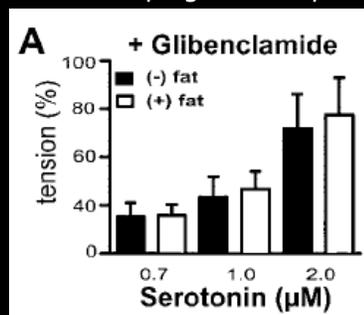
Espécie

PDRF

Resposta anticontrátil

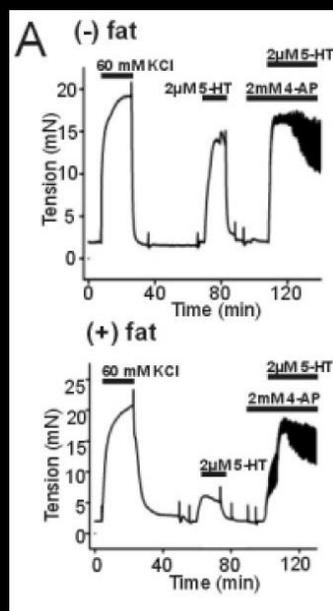
Ação anticontrátil do PVAT: participação dos canais para K⁺

Aorta torácica
Rato Sprague-Dawley



Löhn et al. FASEB J, 16:1057-1063, 2002.

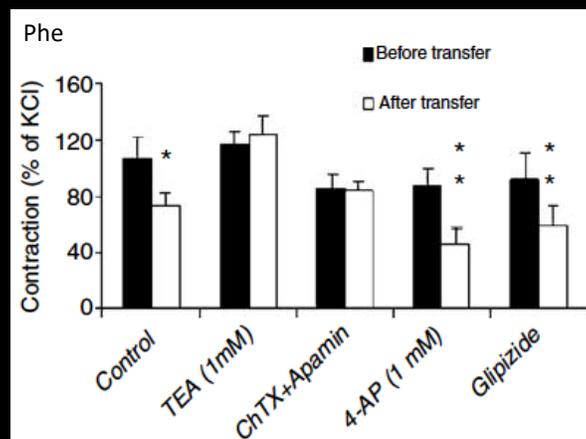
AMS
Rato Sprague-Dawley



Verlohren et al. Hypertension, 44:271-276, 2004.

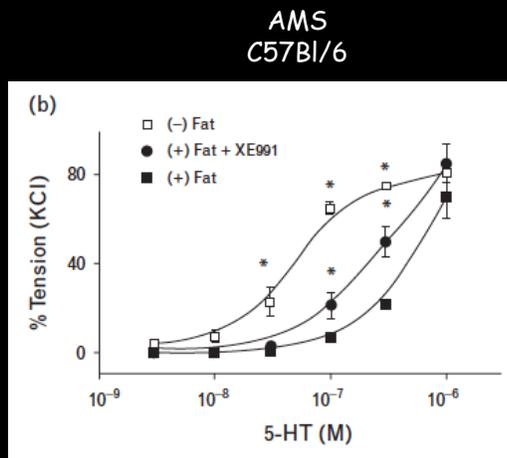
Ação anticontrátil do PVAT: participação dos canais para K⁺

Aorta torácica
Rato Wistar



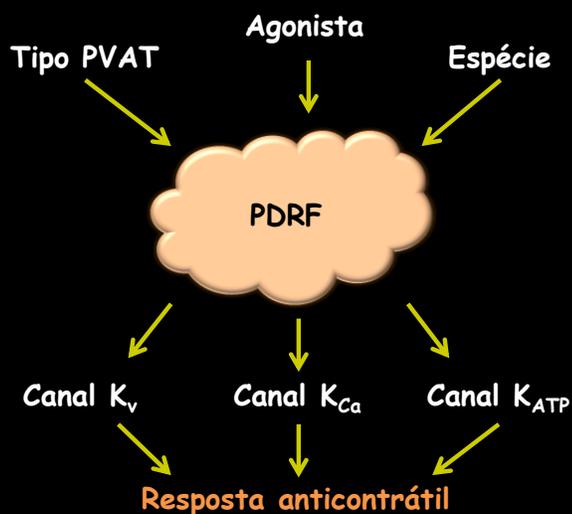
Gao et al. Br J Pharmacol, 151:323, 2007.

Ação anticontrátil do PVAT: participação dos canais para K^+



Schleifnbaum et al. J Hypertens, 28:1875, 2010.

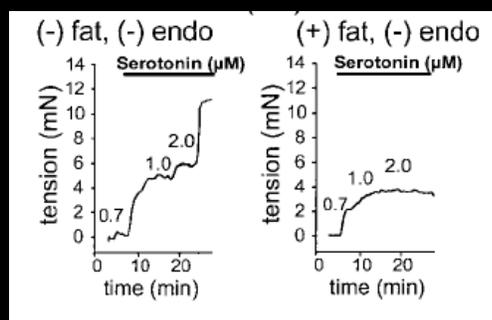
Ação anticontrátil do PVAT: participação dos canais para K^+



Gil-Ortega et al. Trends Endocrinol Metab,26:367-375, 2015.

Ação anticontrátil do PVAT: participação do endotélio

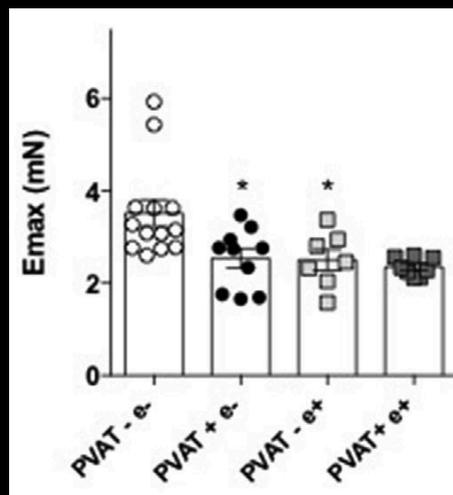
Aorta torácica
Rato Sprague-Dawley



Löhn et al. FASEB J, 16:1057-1063, 2002.

Ação anticontrátil do PVAT: participação do endotélio

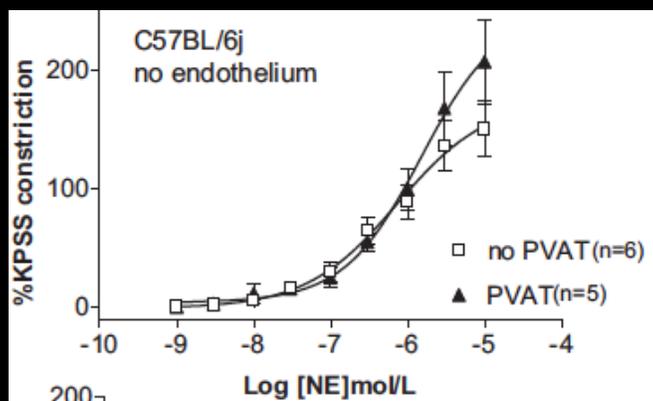
Aorta torácica
Balb/c



Nóbrega et al. Nitric Oxide, 84:50, 2019.

Ação anticontrátil do PVAT: participação do endotélio

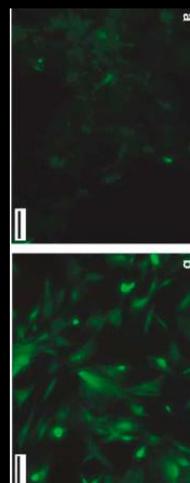
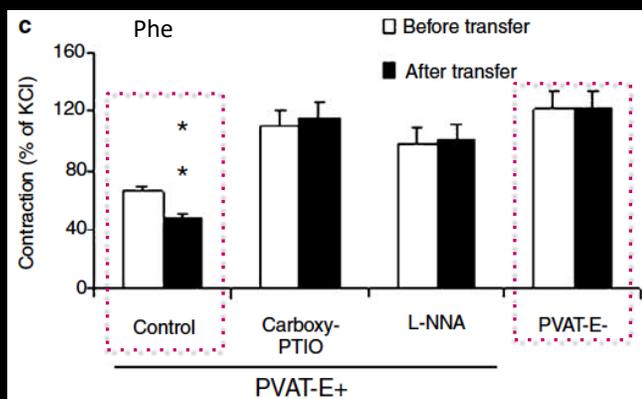
AMR
C57Bl/6



Lynch et al. Am J Physiol, 304:H786, 2013.

Ação anticontrátil do PVAT: participação do endotélio

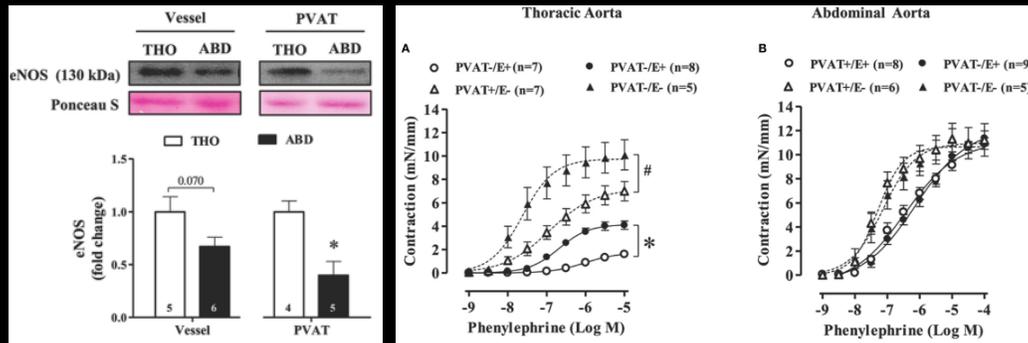
Aorta torácica
Rato Wistar



Gao et al. Br J Pharmacol, 151:323, 2007.

Ação anticontrátil do PVAT: expressão da eNOS no PVAT

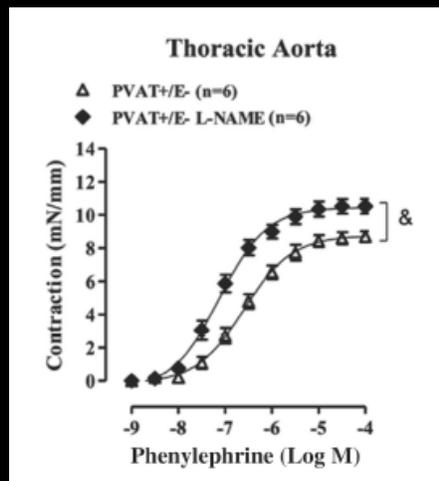
Rato Wistar



Victorio, Fontes et al. Front Physiol, 7:295, 2016.

Ação anticontrátil do PVAT: expressão da eNOS no PVAT

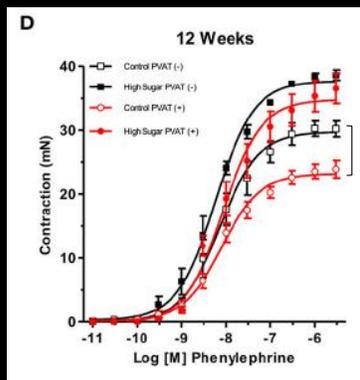
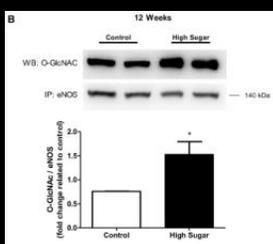
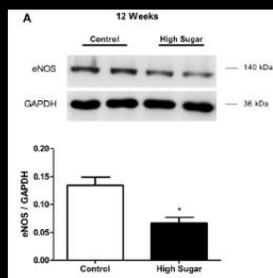
Rato Wistar



Victorio, Fontes et al. Front Physiol, 7:295, 2016.

Ação anticontrátil do PVAT: expressão da eNOS no PVAT

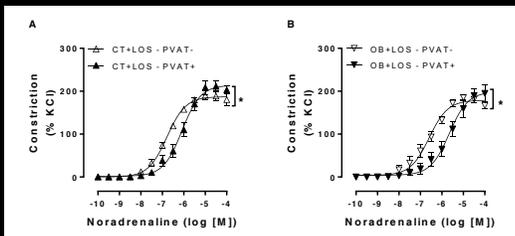
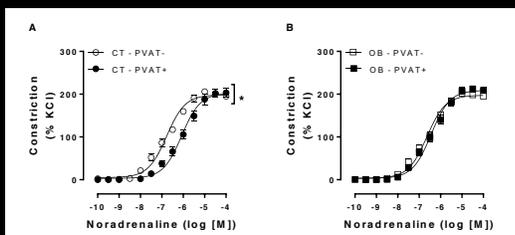
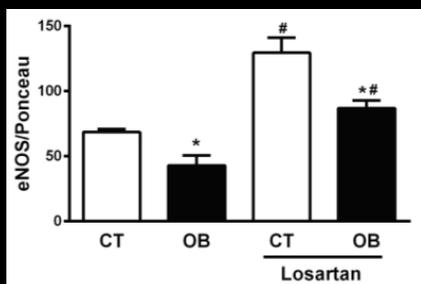
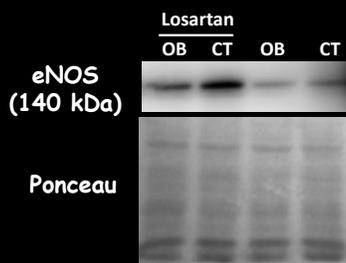
Aorta torácica
Rato Wistar



Costa et al. Front Physiol, 9:341, 2018.

Ação anticontrátil do PVAT: expressão da eNOS no PVAT

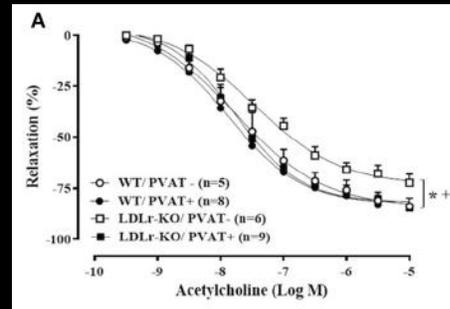
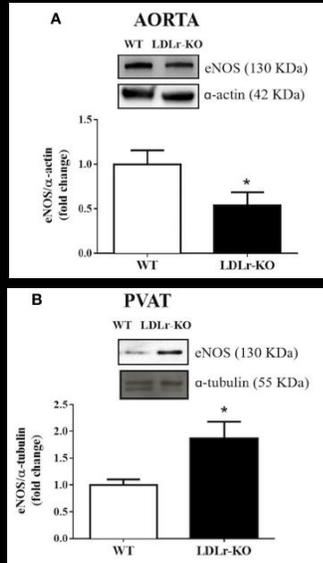
PVAT mesentérico
C57Bl/6



Hashimoto CM, Inada AC, submetido.

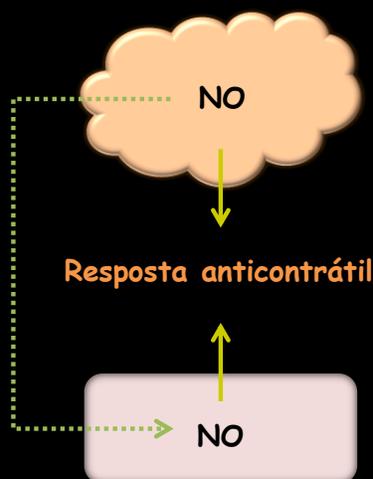
Ação anticontrátil do PVAT: expressão da eNOS no PVAT

Aorta torácica
C57Bl/6



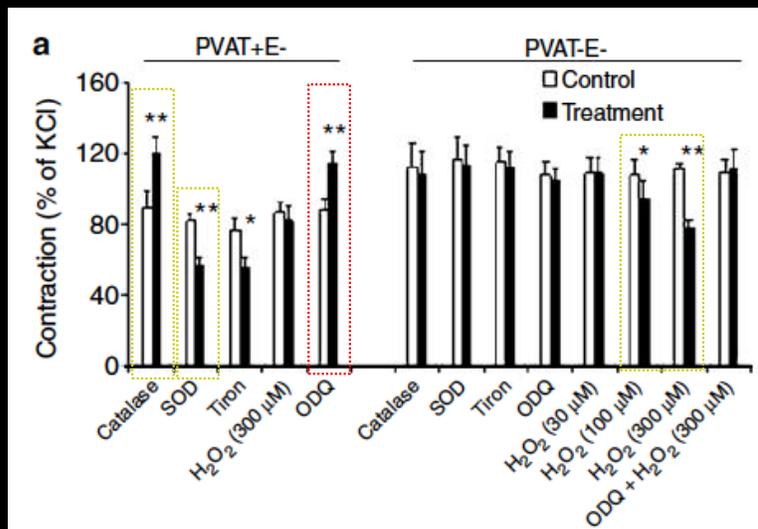
Baltieri et al. Front Physiol, 9:229, 2018.

Ação anticontrátil do PVAT: participação do NO



Ação anticontrátil do PVAT: participação do H₂O₂

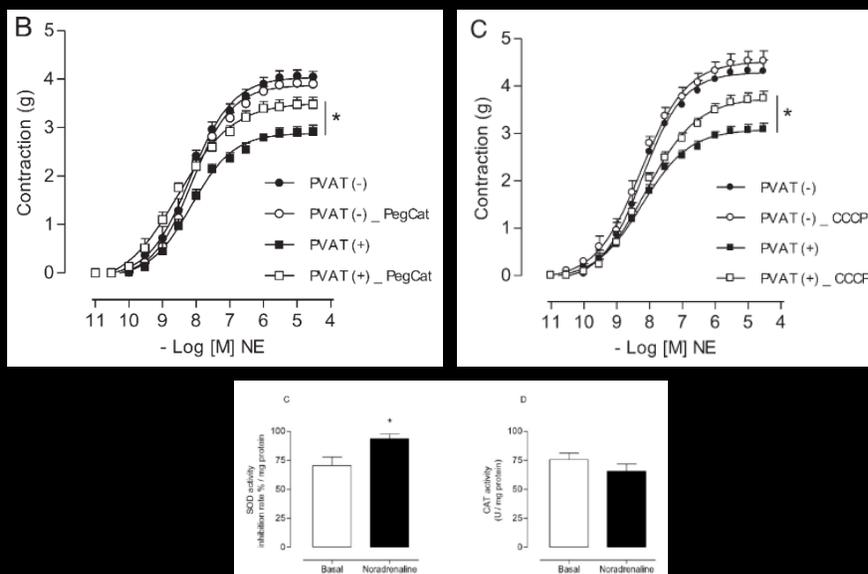
Aorta torácica
Rato Wistar



Gao et al. Br J Pharmacol, 151:323, 2007.

Ação anticontrátil do PVAT: participação do H₂O₂

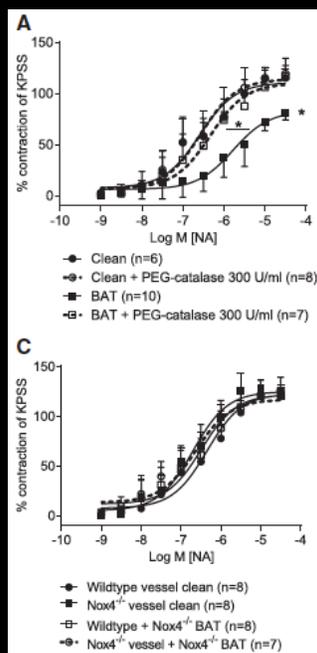
Aorta torácica
Rato Wistar



Costa et al. Vasc Pharmacol, 84:28, 2016.

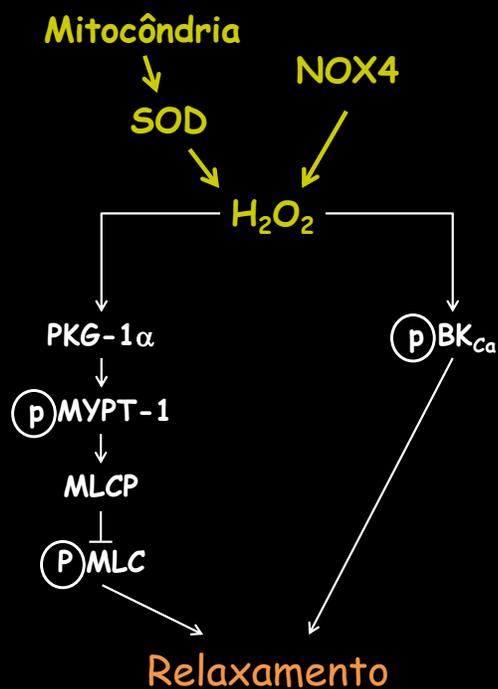
Ação anticontrátil do PVAT: participação do H_2O_2

AMR
C57Bl/6 e FVb



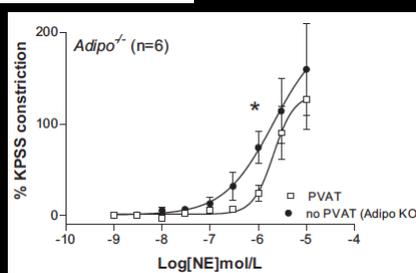
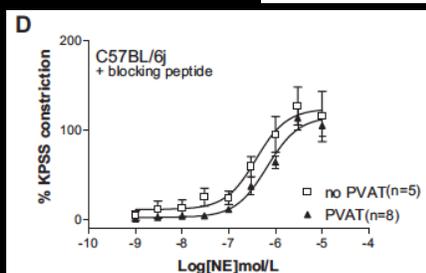
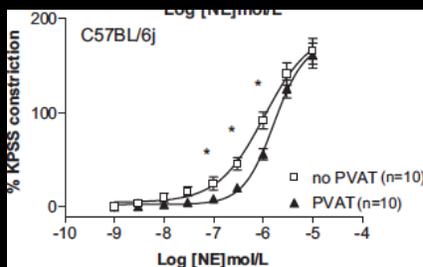
Friederich-Persson et al. Arterioscler Thromb Vasc Biol, 37:455, 2017.

Ação anticontrátil do PVAT: participação do H_2O_2



Ação anticontrátil do PVAT: participação da adiponectina

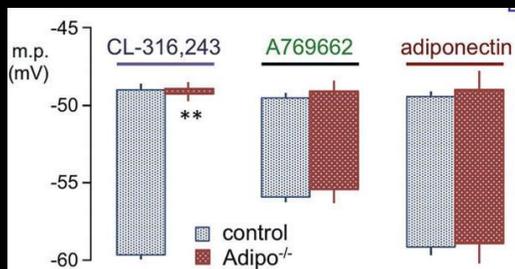
AMR
C57Bl/6



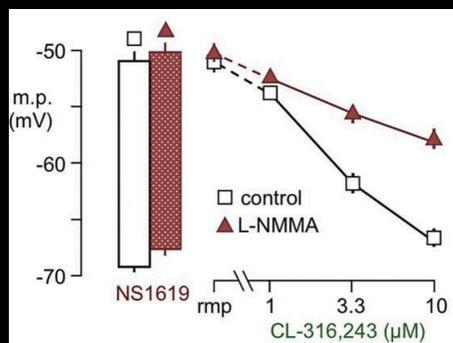
Lynch et al. Am J Physiol, 304:H786, 2013.

Ação anticontrátil do PVAT: participação da adiponectina e AMPK

AMR
C57Bl/6

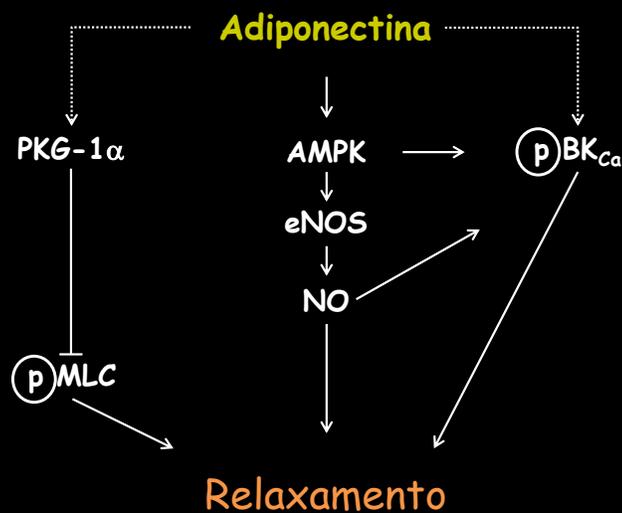


AMR
Rato Sprague-Dawley



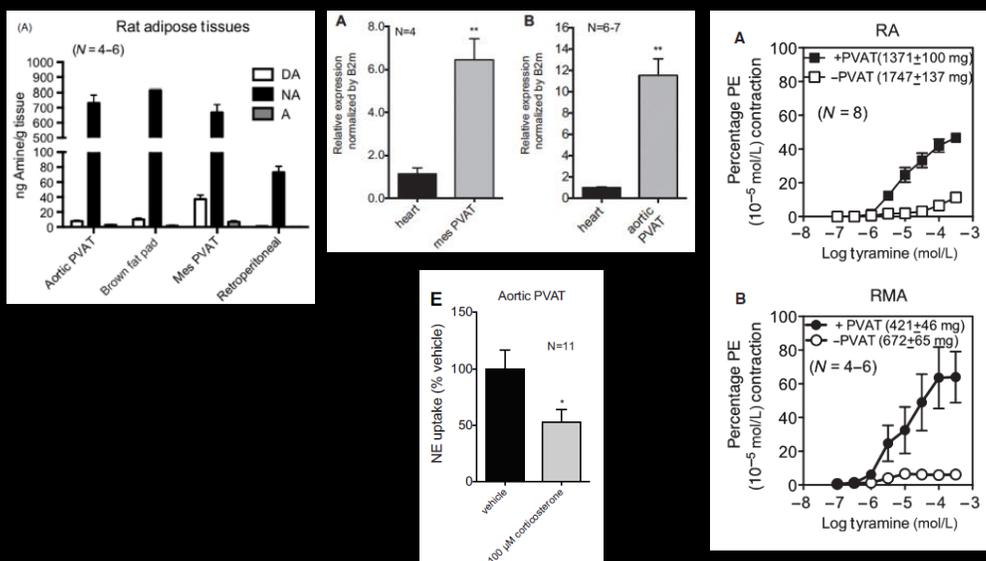
Weston et al. Br J Pharmacol, 169:1500, 2013.

Ação anticontrátil do PVAT: participação da adiponectina



Ação anticontrátil do PVAT: participação da captação de NA

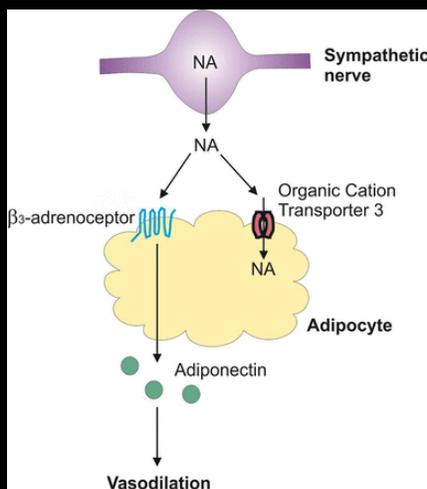
Rato Sprague-Dawley



Ayala-Lopez et al. *Pharma Res Per*, 2:e00041, 2014; Ayala-Lopez et al, *Am J Physiol*, 309:H1904, 2015.

Ação anticontrátil do PVAT: participação da adiponectina

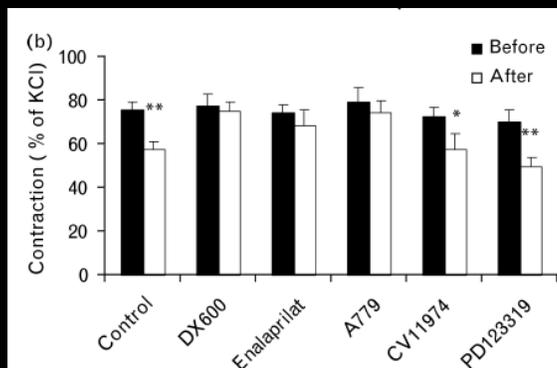
AMR
C57Bl/6



Saxton et al. Arterioscler Thromb Vasc Biol, 38:880, 2018.

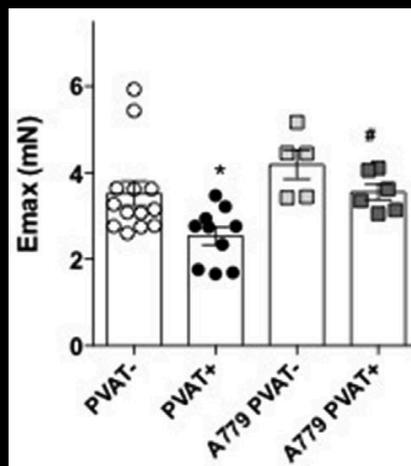
Ação anticontrátil do PVAT: participação do SRA

Aorta torácica
Rato Wistar



Lee et al. J Hypertens, 27:782, 2009.

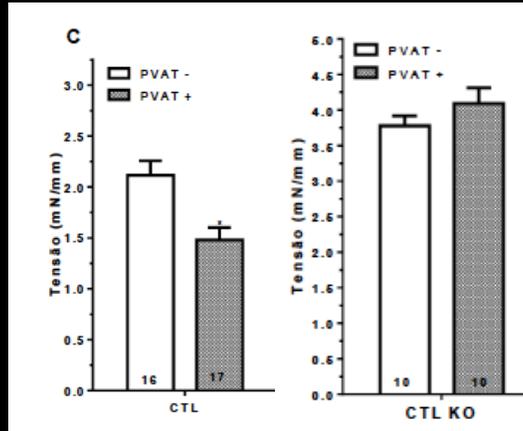
Aorta torácica
Balb/c



Nóbrega et al. Nitric Oxide, 84:50, 2019.

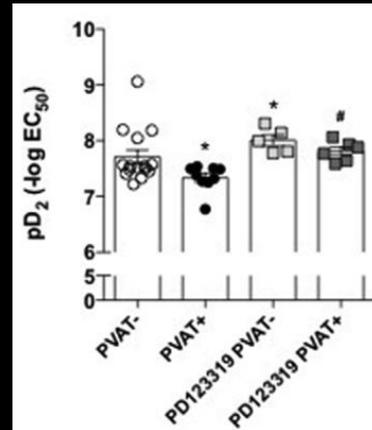
Ação anticontrátil do PVAT: participação do SRA

Aorta torácica
C57Bl6



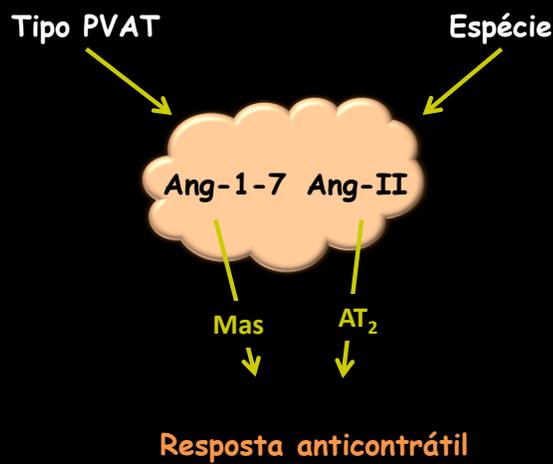
Marques BVD, em preparação.

Aorta torácica
Balb/c

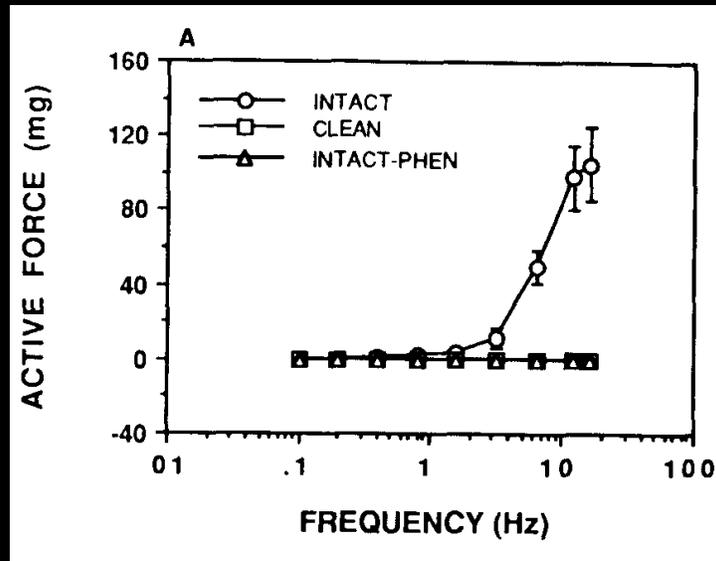


Nóbrega et al. Nitric Oxide, 84:50, 2019.

Ação anticontrátil do PVAT: participação do SRA



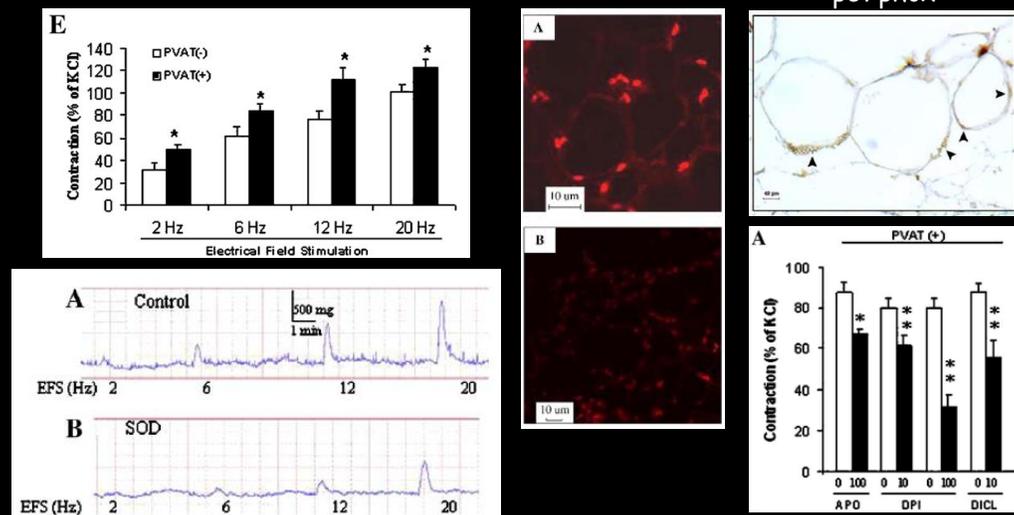
Ação contrátil do PVAT



Soltis e Cassis. Clin Exp Hypertens, 13:277, 1991.

Ação contrátil do PVAT: participação do O_2^-

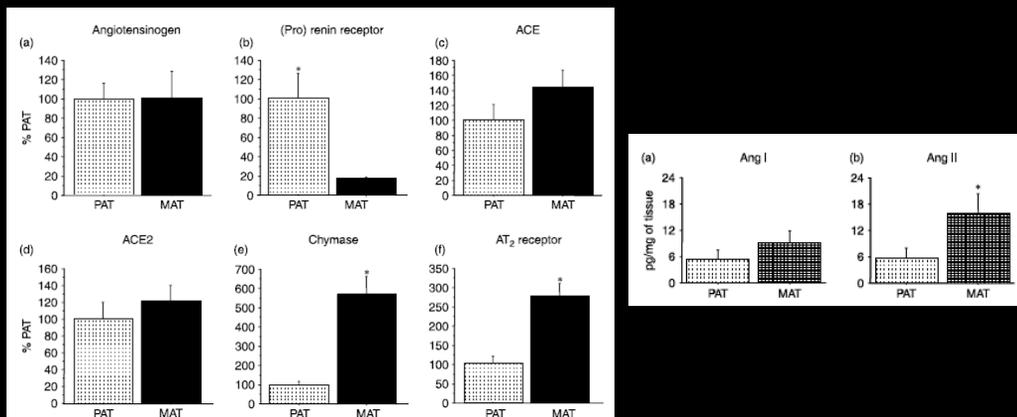
AMS
Rato Wistar-Kyoto



Gao et al. Cardiovasc Res, 71:363, 2007.

Ação contrátil do PVAT: participação do SRAA

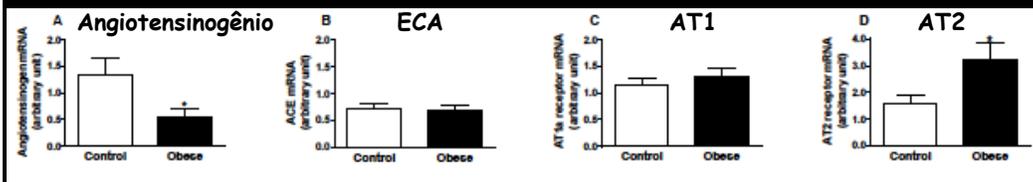
Rato Wistar-Kyoto



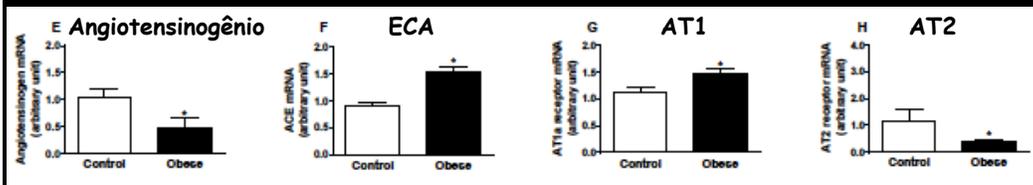
Gálvez-Prieto et al. J Endocrinol, 197:55, 2008.

Ação contrátil do PVAT: participação do SRAA

PVAT - aorta torácica
C57Bl/6



PVAT mesentérico
C57Bl/6

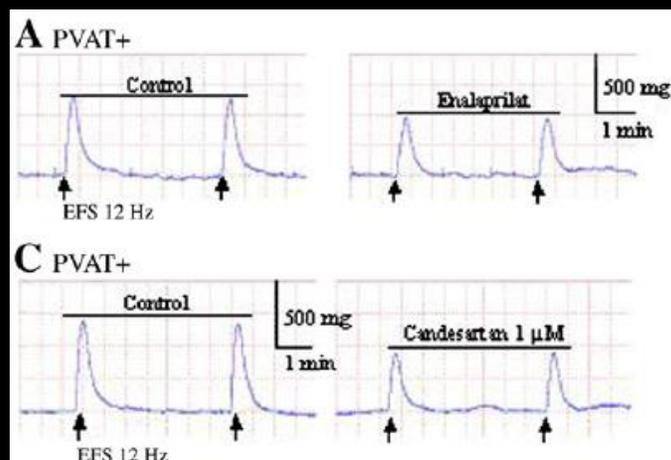


*P<0,05 versus control, n=7.

Hashimoto CM, Inada AC, submetido.

Ação contrátil do PVAT: participação do SRAA

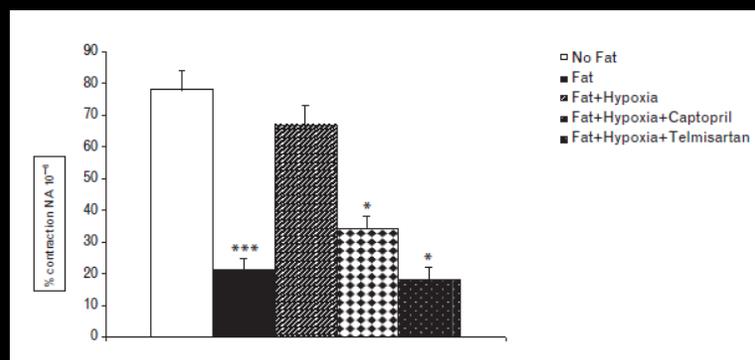
AMS
Rato Wistar



Lu et al. Eur J Pharmacol, 634:107, 2010.

Ação contrátil do PVAT: participação do SRAA

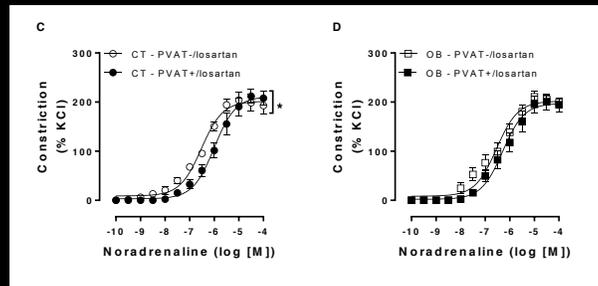
AMR
Rato Sprague-Dawley



Rosei et al. J Hypertens, 33:1039, 2015.

Ação contrátil do PVAT: participação do SRAA

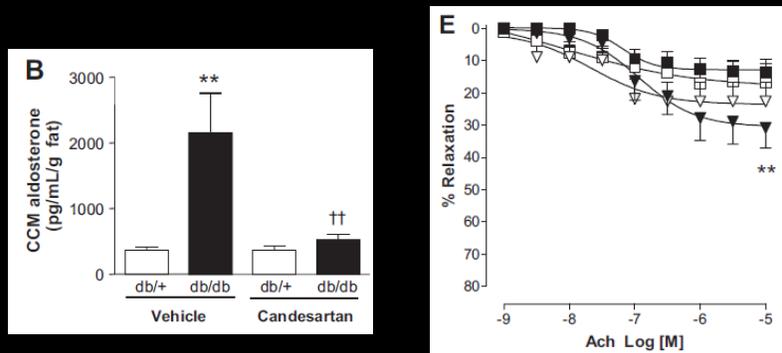
PVAT mesentérico
C57Bl/6



Hashimoto CM, Inada AC, submetido.

Ação contrátil do PVAT: participação do SRAA

AMR
C57Bl/6



Briones et al. Hypertension, 59:1069, 2012.

TECIDO ADIPOSEO PERIVASCULAR

Resumo

- Características e função dependem da localização anatômica e da espécie
- Mediadores relaxantes e contráteis: equilíbrio determina ação final
- Interação com o endotélio

TECIDO ADIPOSEO PERIVASCULAR

Perspectivas

Entender os mecanismos envolvidos nas ações do PVAT, considerando as diferentes características e origem.

Entender a regulação da liberação dos mediadores.

Entender a interação com o endotélio, inervações e células imunológicas e tronco-mesenquimais.