

UNIVERSIDADE FEDERAL DE UBERLÂNDIA**Ficha de Disciplina****DISCIPLINA:** Aspectos celulares, moleculares e funcionais das células endoteliais e do músculo liso vascular.

PERÍODO:	CURSO: Programa de Pós-graduação em Biologia Celular e Estrutural Aplicadas		DEPARTAMENTO: Departamento de Farmacologia – DEFAR.
CÓDIGO : PBC-040	CH: : 45 horas	CR: 3 créditos	Mestrado: optativa

Requisitos (disciplinas pré ou co-requisitos, nº de créditos, outros) – sem pré-requisitos**Objetivos gerais da disciplina**

O tônus vascular determina o fluxo sanguíneo regional e participa na manutenção da pressão arterial; ele é modulado por fatores intrínsecos e extrínsecos aos vasos sanguíneos. Dentre os fatores extrínsecos podem ser citados os hormônios circulantes e a tensão de cisalhamento imposta pela corrente circulatória. Por outro lado, a produção local de substâncias dilatadoras e constritoras, principalmente pelas células endoteliais, constitui o principal fator intrínseco relacionado à manutenção do tônus vascular. A intervenção farmacológica desse processo constitui importante abordagem terapêutica em diversas doenças. Considerando a relevância do tema, a presente disciplina tem por objetivos propiciar a aquisição de conhecimentos fundamentais sobre a fisiologia, bioquímica e farmacologia das células endoteliais e da musculatura lisa vascular.

Ementa do programa

1. Fisiologia da contração do músculo liso vascular.
2. Mecanismos de transdução do sinal nas células endoteliais e na musculatura lisa vascular.
3. Fatores de relaxamento e de contração derivados do endotélio.
4. Disfunção endotelial.
5. Intervenção farmacológica do tônus muscular.
6. Considerações metodológicas no estudo do tônus vascular.

Bibliografia

1. Akata T. Cellular and molecular mechanisms regulating vascular tone. Part 2: regulatory mechanisms modulating Ca²⁺ mobilization and/or myofilament Ca²⁺ sensitivity in vascular smooth muscle cells. *J Anesth.* 2007;21(2):232-42.
2. Akata T. Cellular and molecular mechanisms regulating vascular tone. Part 1: basic mechanisms controlling cytosolic Ca²⁺ concentration and the Ca²⁺-dependent regulation of vascular tone. *J Anesth.* 2007;21(2):220-31.
3. Furchtgott RF, Vanhoutte PM. Endothelium-derived relaxing and contracting actors. *FASEB J.* 1989 Jul;3(9):2007-18.
4. Fleming I, Busse R. NO: the primary EDRF. *J Mol Cell Cardiol.* 1999 Jan;31(1):5-14.
5. Féletalou M, Huang Y, Vanhoutte PM. Vasoconstrictor prostanoids. *Pflugers Arch.* 2010 May;459(6):941-50.
6. Féletalou M, Huang Y, Vanhoutte PM. Endothelium-mediated control of vascular tone: COX-1 and COX-2 products. *Br J Pharmacol.* 2011 Oct;164(3):894-912.
7. Busse R, Edwards G, Féletalou M, Fleming I, Vanhoutte PM, Weston AH. EDHF: bringing the concepts together. *Trends Pharmacol Sci.* 2002 Aug;23(8):374-80.
8. Wulff H, Köhler R. Endothelial small-conductance and intermediate-conductance KCa channels: an update on their pharmacology and usefulness as cardiovascular targets. *J Cardiovasc Pharmacol.* 2013 Feb;61(2):102-12.
9. Féletalou M, Vanhoutte PM. EDHF: an update. *Clin Sci (Lond).* 2009 Jul 16;117(4):139-55.
10. Rubanyi GM. The discovery of endothelin: the power of bioassay and the role of serendipity in the discovery of endothelium-derived vasoconstrictive substances. *Pharmacol Res.* 2011 Jun;63(6):448-54.
11. Davenport AP, Hyndman KA, Dhaun N, Southan C, Kohan DE, Pollock JS, Pollock DM, Webb DJ, Maguire JJ. Endothelin. *Pharmacol Rev.* 2016 Apr;68(2):357-418.
12. Tobe S, Kohan DE, Singarayer R. Endothelin Receptor Antagonists: New Hope for Renal Protection? *Curr Hypertens Rep.* 2015 Jul;17(7):57.
13. Clozel M, Maresta A, Humbert M. Endothelin receptor antagonists. *Handb Exp Pharmacol.* 2013;218:199-227.
14. Wallez Y, Huber P. Endothelial adherens and tight junctions in vascular homeostasis, inflammation and angiogenesis. *Biochim Biophys Acta.* 2008 Mar;1778(3):794-809.
15. Reglero-Real N, Colom B, Bodkin JV, Nourshargh S. Endothelial Cell Junctional Adhesion Molecules: Role and Regulation of Expression in Inflammation. *Arterioscler Thromb Vasc Biol.* 2016 Oct;36(10):2048-57.
16. Tzima E, Irani-Tehrani M, Kiosses WB, Dejana E, Schultz DA, Engelhardt B, Cao G, DeLisser H, Schwartz MA. A mechanosensory complex that mediates the endothelial cell response to fluid shear stress. *Nature.* 2005 Sep 15;437(7057):426-31.
17. Yamamoto K, Ando J. New molecular mechanisms for cardiovascular disease: blood flow sensing mechanism in vascular endothelial cells. *J Pharmacol Sci.* 2011;116(4):323-31. Epub 2011 Jul 14.
18. Sowa G. Caveolae, caveolins, cavins, and endothelial cell function: new insights. *Front Physiol.* 2012 Jan 6;2:120.
19. Watanabe T, Barker TA, Berk BC. Angiotensin II and the endothelium: diverse signals and effects. *Hypertension.* 2005 Feb;45(2):163-9.
20. Fleming I. Signaling by the angiotensin-converting enzyme. *Circ Res.* 2006 Apr 14;98(7):887-96.
21. Fleming I, Kohlstedt K, Busse R. New fACES to the renin-angiotensin system. *Physiology.*

- (Bethesda). 2005 Apr;20:91-5.
22. Li JM, Shah AM. Mechanism of endothelial cell NADPH oxidase activation by angiotensin II. Role of the p47phox subunit. *J Biol Chem*. 2003 Apr 4;278(14):12094-100.
 23. Féletalou M, Vanhoutte PM. Endothelial dysfunction: a multifaceted disorder (The Wiggers Award Lecture). *Am J Physiol Heart Circ Physiol*. 2006 Sep;291(3):H985-1002.
 24. Kershaw KN, Lane-Cordova AD, Carnethon MR, Tindle HA, Liu K. Chronic Stress and Endothelial Dysfunction: The Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Hypertens*. 2017 Jan;30(1):75-80. Epub 2016 Sep 1.
 25. Shimbo D, Muntner P, Mann D, Viera AJ, Homma S, Polak JF, Barr RG, Herrington D, Shea S. Endothelial dysfunction and the risk of hypertension: the multi-ethnic study of atherosclerosis. *Hypertension*. 2010 May;55(5):1210-6.
 26. Sena CM, Pereira AM, Seiça R. Endothelial dysfunction - a major mediator of diabetic vascular disease. *Biochim Biophys Acta*. 2013 Dec;1832(12):2216-31.
 27. Avogaro A, Albiero M, Menegazzo L, de Kreutzenberg S, Fadini GP. Endothelial dysfunction in diabetes: the role of reparatory mechanisms. *Diabetes Care*. 2011 May;34 Suppl 2:S285-90.
 28. Lobato NS, Filgueira FP, Akamine EH, Tostes RC, Carvalho MH, Fortes ZB. Mechanisms of endothelial dysfunction in obesity-associated hypertension. *Braz J Med Biol Res*. 2012 May;45(5):392-400.
 29. DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. *Nat Rev Endocrinol*. 2014 Jun;10(6):364-76.
 30. Sozen AB, Kayacan MS, Tansel T, Celebi A, Kudat H, Akkaya V, Erk O, Hatipoglu I, Demirel S. Drugs with blocking effects on the renin-angiotensin-aldosterone system do not improve endothelial dysfunction long-term in hypertensive patients. *J Int Med Res*. 2009 Jul-Aug;37(4):996-1002.
 31. Treuer AV, Gonzalez DR. Nitric oxide synthases, S-nitrosylation and cardiovascular health: from molecular mechanisms to therapeutic opportunities (review). *Mol Med Rep*. 2015 Mar;11(3):1555-65.
 32. Vanhoutte PM, Shimokawa H, Feletou M, Tang EH. Endothelial dysfunction and vascular disease - a 30th anniversary update. *Acta Physiol (Oxf)*. 2017 Jan;219(1):22-96. doi: 10.1111/apha.12646.
 33. Fleming I. The factor in EDHF: Cytochrome P450 derived lipid mediators and vascular signaling. *Vascul Pharmacol*. 2016 Nov;86:31-40.
 34. Kalyanaraman B. Teaching the basics of redox biology to medical and graduate students: Oxidants, antioxidants and disease mechanisms. *Redox Biol*. 2013 Feb 8;1:244-57.
 35. Garland CJ, Dora KA. EDH: endothelium-dependent hyperpolarization and microvascular signalling. *Acta Physiol (Oxf)*. 2017 Jan;219(1):152-161.

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PROEPE 408

Descrição do programa

Mecanismos envolvidos na contração e relaxamento da musculatura lisa vascular.

Endotélio e tônus vascular: aspectos gerais.

Endotélio: óxido nítrico.

Endotélio: prostanoides e hiperpolarização derivada do endotélio.

Endotélio: endotelinas e junções.

Endotélio: sensores mecânicos e regiões especializadas da membrana.

Endotélio e o sistema renina-angiotensina-aldosterona.

Disfunção endothelial.

Métodos empregados no estudo do tônus vascular.