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The Role of Calcium-Sensing Receptors in Endothelin---Dependent Effects on Adult Rat Ventricular Cardiomyocytes: Possible Contribution to Adaptive Myocardial Hypertrophy

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Abstract

© 2016 Wiley Periodicals, Inc. Nitric oxide (NO)-deficiency as it occurs during endothelial dysfunction activates the endothelin-1 (ET-1) system and increases the expression of receptor activity modifying protein (RAMP)-1 that acts as a chaperon for calcium-sensing receptors (CaR) that have recently been identified to improve cardiac function. Here, we hypothesized that ET-1 increases the cardiac expression of CaR and thereby induces an adaptive type of hypertrophy. Expressions of RAMP-1, endothelin receptors, and CaR were analyzed by RT-PCR in left ventricular tissues of L-NAME-treated rats. Effects of ET-1 on CaR expression and cell function (load free cell shortening) were analyzed in adult rat ventricular cardiomyocytes. siRNA directed against CaR and RAMP-1 was used to investigate a causal relationship. PD142893 and BQ788 were used to dissect the contribution of ET B1 , ET B2 , and ET A receptors. Non-specific NO synthase inhibition with L-Nitro arginine methyl ester (L-NAME) caused a cardiac upregulation of ET B receptors and CaR suggesting a paracrine effect of ET-1 on cardiomyocytes. Indeed, ET-1 induced the expression of CaR in cultured cardiomyocytes. Under these conditions, cardiomyocytes increased cell size (hypertrophy) but maintained normal function. Inhibition of ET A and ET B1 receptors led to ET-1-dependent reduction in cell shortening and attenuated up-regulation of CaR. Down-regulation of RAMP-1 reduced CaR responsiveness. In conclusion, ET-1 causes an adaptive type of hypertrophy by up-regulation of CaR in cardiomyocytes via ET A and/or ET B1 receptors. J. Cell. Physiol. 232: 2508–2518, 2017. © 2016 Wiley Periodicals, Inc.

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References

[1] Anwar A, Schlüter KD, Heger J, Piper HM, Euler G. 2008. Enhanced SERCA2A expression improves contractile performance of ventricular cardiomyocytes of rat under adrenergic stimulation. Eur J Physiol 457:485–491.

[2] Bartolome JV, Guguenard J, Slotkin TA. 1980. Role of ornithine decarboxylase in cardiac growth and hypertrophy. Science 210:793–794.

[3] Bouschet T, Martin S, Henley JM. 2005. Receptor-activity-modifying proteins are required for forward trafficking of the calcium-sensing receptor to the plasma membrane. J Cell Sci 118:4709–4720.

[4] Bras-Silva C, Fontes-Sousa AP, Moura C, Areias JC, Leite-Moreira AF. 2006. Impaired response to ET(B) receptor stimulation in heart failure: Functional evidence of endocardial endothelial dysfunction? Exp Biol Med (Maywood) 231:893–898.

[5] Brunner F, Stessel H, Kukovetz WR. 1995. Novel guanylyl cyclase inhibitor, ODQ reveals role of nitric oxide, but not of cyclic GMP in endothelin-1 secretion. FEBS Lett 376:262–266.

[6] Cai H, Harrison DG. 2000. Endothelial dysfunction in cardiovascular diseases: The role of oxidant stress. Circ Res 87:840–844.

[7] Caldarera CM, Casti A, Rossoni C, Visioli O. 1971. Polyamines and noradrenaline following myocardialhypertrophy. J Mol Cell Cardiol 3:121–126.

[8] Dong S, Teng Z, Lu FH, Zhao YJ, Li H, Ren H, Chen H, Pan ZW, Lv YJ, Yang BF, Tian Y, Xu CQ, Zhang WH. 2010. Post-conditioning protects cardiomyocytes from apoptosis via PKC(epsilon)-interacting with calcium-sensing receptors to inhibit endo(sarco)plasmatic reticulum-mitochondria crosstalk. Mol Cell Biochem 341:195–206.

[9] Drimal J, Knezl V, Drimal J, Jr., Drímal D, Bauerova K, Kettmann V, Doherty AM, Stefek M. 2003. Cardiac effects of endothelin-1 (ET-1) and related C-terminal peptide fragment: Increased inotropy or contribution to heart failure? Physiol Res 52:701–708.

[10] Gan R, Hu G, Zhao Y, Li H, Jin Z, Ren H, Dong S, Zhong X, Li H, Yang B, Xu C, Lu F, Zhang W. 2012. Post-conditioning protecting rat cardiomyocytes from apoptosis via attenuated calcium-sensing receptor-induced endo(sarco)plasmic reticulum stress. Mol Cell Biochem 361:123–134.

[11] Hinrichs S, Heger J, Schreckenberg R, Wenzel S, Euler G, Arens C, Bader M, Rosenkranz S, Caglayan E, Schlüter KD. 2011. Controlling cardiomyocyte length: Role of renin and PPAR-gamma. Cardiovasc Res 89:344–352.

[12] Hoeper MM. 2009. Liver toxicity: The Achilles' heel of endothelin receptor antagonist therapy? Eur Respir J 34:529–530.

[13] Hofer AM, Brown EM. 2003. Extracellular calcium sensing and signalling. Nat Rev Mol Cell Biol 4:530–538.

[14] Hsu YH, Hsu BG, Chen HI. 2008. Malignant alterations following early blockade of nitric oxide synthase in hypertensive rats. Chin J Physiol 50:283–293.

[15] Jones LG, Rozich JD, Tsutsui H, Cooper G, 4th. 1992. Endothelin stimulates multiple responses is isolated adult ventricular cardiac myocytes. Am J Physiol 263:H1447–H1454.

[16] Lee GR, Bell D, Kelso EJ, Argent CC, McDermott BJ. 2004. Evidence for altered ETB receptor characteristics during development and progression of ventricular cardiomyocyte hypertrophy. Am J Physiol Heart Circ Physiol 287:H425–H432.

[17] McLatchie LM, Fraser NJ, Main MJ, Wise A, Brown J, Thompson N, Solari R, Lee MG, Foord SM. 1998. RAMPs regulate the transport and ligand specificity of the calcitonin-receptor-like receptor. Nature 393:333–339.

[18] Pegg AE, Hibasami H. 1980. Polyamine metabolism during cardiac hypertrophy. Am J Physiol 239:E372–E378.

[19] Penna C, Rastaldo R, Mancardi D, Cappello S, Pagliaro P, Westerhof N, Losano G. 2006. Effect of endothelins on the cardiovascular system. J Cardiovasc Med (Hagerstown) 7:645–652.

[20] Sato A, Ebina K. 2013. Endothelin-3 at low concentrations attenuates inflammatory responses via the endothelin B2 receptor. Inflamm Res 62:417–424.

[21] Schreckenberg R, Dyukova E, Sitdikova G, Abdallah Y, Schlüter KD. 2015a. Mechanisms by which calcium receptor stimulation modifies electromechanical coupling in isolated ventricular cardiomyocytes. Pflugers Arch 467:379–388.

[22] Schreckenberg R, Rebelo M, Deten A, Weber M, Rohrbach S, Pipicz M, Csonka C, Ferdinandy P, Schulz R, Schlüter KD. 2015b. Specific mechanisms underlying right heart failure: The missing upregulation of superoxide dismutase-2 and its decisive role in antioxidative defense. Antioxid Redox Signal 23:1220–1232.

[23] Schlüter KD, Schreiber D. 2005. Adult ventricular cardiomyocytes: Isolation and culture. Methods Mol Biol 290:305–314.

[24] Thakali KM, Lau Y, Fink GD, Galligan JJ, Chen AF, Watts SW. 2006. Mechanisms of hypertension induced by nitric oxide (NO) deficiency: Focus on venous function. J Cardiovasc Pharmacol 47:742–750.

[25] Tfelt-Hansen J, Hansen JL, Smajilovic S, Terwilliger EF, Haunso S, Sheikh SP. 2006. Calcium receptor is functionally expressed in rat neonatal ventricular cardiomyocytes. Am J Physiol Heart Circ Physiol 290:H1165–H1171.

[26] Tfelt-Hansen J, Schwarz P, Brown EM, Chattopadhyay N. 2003. The calcium-sensing receptor in human disease. Front Biosci 8:s377–s390.

[27] Wang LN, Wang C, Lin Y, Xi YH, Zhang WH, Zhao YJ, Li HZ, Tian Y, Lv YJ, Yang BF, Xu CQ. 2008. Involvement of calcium-sensing receptor in cardiac hypertrophy-induced by angiotensin II through calcineurin pathway in cultured neonatal rat cardiomyocytes. Biochem Biophys Res Commun 369:584–589.

[28] Warner TD, Allcock DH, Corder R, Vane JR. 1993. Use of the endothelin antagonists BQ-123 and PD142893 to reveal three different endothelin receptors mediating smooth muscle contraction and the release of EDRF. Br J Pharmacol 117:777–782.

[29] Wenzel S, Tastan I, Abdallah Y, Schreckenberg R, Schlüter KD. 2010. Aldosterone improves contractile function of adult rat ventricular cardiomyocytes in a non-acute way: Potential relationship to the calcium paradox of aldosteronism. Basic Res Cardiol 105:247–256.

[30] Zhao Y, Bell D, Smith LR, Zhao L, Devine AB, McHenry EM, Nicholls DP, McDermott BJ. 2006. Differential expression of components of the cardiomyocytes adrenomedullin/intermedin receptor system following blood pressure reduction in nitric oxide-deficient hypertension. J Pharmacol Exp Ther 316:1269–1281.

[31] Zhao YJ, Xu CQ, Zhang WH, Zhang L, Bian SL, Huang Q, Sun HL, Li QF, Zhang YQ, Tian Y, Wang R, Yang BF, Li WM. 2007. Role of polyamines in myocardial ischemia/reperfusion injury and their interactions with nitric oxide. Eur J Pharmacol 562:236–246.