AMPK alpha 1-induced RhoA phosphorylation mediates vasoprotective effect of estradiol

Titre	AMPK alpha 1-induced RhoA phosphorylation mediates vasoprotective effect of estradiol
Type de publication	Article de revue
Auteur	Gayard, M. [1], Guilluy, C. [2], Rousselle, A. [3], Viollet, B. [4], Henrion, Daniel [5], Pacaud, Pierre [6], Loirand, Gervaise [7], Rolli-Derkinderen, M. [8]
Editeur	American Heart Association
Type	Article scientifique dans une revue à comité de lecture
Année	2011
Langue	Anglais
Date	2011
Numéro	11
Pagination	2634 - 42
Volume	31
Titre de la revue	Arteriosclerosis, Thrombosis, and Vascular Biology
ISSN	1524-4636
Mots-clés	AMP-Activated Protein Kinases/genetics/metabolism [9], Animals [10], Cells, Cultured [11], Dose-Response Relationship, Drug [12], Estradiol/pharmacology [13], Female [14], Male [15], Mice [16], Mice, Knockout [17], Models, Animal [18], Muscle, Smooth, Vascular/cytology/drug effects/metabolism [19], Ovariectomy [20], Phosphorylation/drug effects [21], Receptors, Estrogen/metabolism [22], rho GTP-Binding Proteins/metabolism [23], rho-Associated Kinases/antagonists & inhibitors/metabolism [24], Signal Transduction/drug effects [25], Time Factors [26], Vasoconstriction/physiology [27]

Résumé en anglais	OBJECTIVE: Estradiol (E2) mediates numerous beneficial effects assigned to estrogens, but whereas mechanisms have been described at the endothelial level, direct effects on vascular smooth muscle cells (VSMC) are poorly documented. As evidence accumulates regarding the role of RhoA in vascular pathophysiology and the benefit of RhoA-Rho associated protein kinase (Rock) pathway inhibition, we analyzed if E2 could inhibit it in VSMC. METHODS AND RESULTS: We show that in VSMC, E2 inhibits the RhoA-Rock pathway in a time- and concentration-dependent manner. The inhibition of RhoA-Rock pathway results from E2-induced phosphorylation of the Ser188 of RhoA. Using pharmacological, transfection, and in vitro phosphorylation experiments, we demonstrate that AMP-activated protein kinase subunit alpha 1 (AMPKalpha1) is activated by estrogen receptor stimulation and catalyzes RhoA phosphorylation induced by E2. Ex vivo, ovariectomy leads to an increase in the amplitude of phenylephrine- or serotonine-induced contractions of aortic rings in wild-type mice but not in AMPKalpha1-knock-out mice or E2-supplemented animals. These functional effects were correlated with a reduced level of RhoA phosphorylation in the aorta of ovariectomized female, male, and AMPKalpha1 knock-out mice. CONCLUSION: Our work thus defines AMPKalpha1 as (1) a new kinase for RhoA and (2) a new mediator of the vasoprotective effects of estrogen.
URL de la notice	http://okina.univ-angers.fr/publications/ua8162 [28]
DOI	10.1161/ATVBAHA.111.228304 [29]
Lien vers le document	http://dx.doi.org/10.1161/ATVBAHA.111.228304 [29]
Titre abrégé	Arterioscler Thromb Vasc Biol

Liens

[1] http://okina.univ-angers.fr/publications?f[author]=13478
[2] http://okina.univ-angers.fr/publications?f[author]=13479
[3] http://okina.univ-angers.fr/publications?f[author]=13480
[4] http://okina.univ-angers.fr/publications?f[author]=13481
[5] http://okina.univ-angers.fr/d.henrion/publications
[6] http://okina.univ-angers.fr/publications?f[author]=17371
[7] http://okina.univ-angers.fr/publications?f[author]=130
[8] http://okina.univ-angers.fr/publications?f[author]=13483
[9] http://okina.univ-angers.fr/publications?f[keyword]=12793
[10] http://okina.univ-angers.fr/publications?f[keyword]=964
[11] http://okina.univ-angers.fr/publications?f[keyword]=1428
[12] http://okina.univ-angers.fr/publications?f[keyword]=1416
[13] http://okina.univ-angers.fr/publications?f[keyword]=12794
[14] http://okina.univ-angers.fr/publications?f[keyword]=1075
[15] http://okina.univ-angers.fr/publications?f[keyword]=968
[16] http://okina.univ-angers.fr/publications?f[keyword]=1102
[17] http://okina.univ-angers.fr/publications?f[keyword]=1147
[18] http://okina.univ-angers.fr/publications?f[keyword]=1434
[19] http://okina.univ-angers.fr/publications?f[keyword]=12795
[20] http://okina.univ-angers.fr/publications?f[keyword]=12796
[21] http://okina.univ-angers.fr/publications?f[keyword]=11406
[22] http://okina.univ-angers.fr/publications?f[keyword]=12797
[23] http://okina.univ-angers.fr/publications?f[keyword]=12799
[24] http://okina.univ-angers.fr/publications?f[keyword]=12798

[25] http://okina.univ-angers.fr/publications?f[keyword]=11408
[26] http://okina.univ-angers.fr/publications?f[keyword]=6070
[27] http://okina.univ-angers.fr/publications?f[keyword]=12800
[28] http://okina.univ-angers.fr/publications/ua8162
[29] http://dx.doi.org/10.1161/ATVBAHA.111.228304