

Diabetes is associated with functional alterations in rat and human penile vascular tissue through Orai channels.

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VI Congreso de Señalización Celular, SECUAH 2021.

29 de marzo a 30 de abril, 2021. Universidad de Alcalá. Alcalá de Henares, Madrid. España.

Keywords: corpus cavernosum; human penile arteries; diabetes; erectile dysfunction; Orai channels; store-operated calcium entry

Abstract

Diabetic patients with erectile dysfunction (ED) are resistant to the conventional treatment of ED. Store-Operated Calcium Entry (SOCE) and its key players, stromal molecule (STIM) and Orai calcium channels, have been proposed as emergent therapeutic targets in cardiovascular pathophysiology and ED. The main objective of this project is to determine the influence of diabetes on the STIM/Orai system in cavernosal tissue from rats and patients with ED at functional and expression level. Rat corpus cavernosum (RCC) from rats with induced insulin-dependent diabetes, and human penile resistance arteries (HPRA) and corpus cavernosum (HCC) from 44 ED patients, who underwent penile prosthesis insertion, were divided into with (n=19) and without (n=25) type 2 diabetes and evaluated in wire myographs and/or organ chambers in presence of Orai channels inhibitors. Expression of STIM-1, Orai-1 and Orai-3 were determined by western blot and immunofluorescence in rat penis and human cavernosal tissues. Corpus cavernosum from diabetic rats displayed hypercontractility to norepinephrine (NE) (E_{max} 119.45±6.55% of K⁺ for NoDM, n=6, vs. 153.12±10.48% of K⁺ for DM, n=5, p< 0.05). YM-58483 did not modify relaxations induced by the NO donor, sodium nitroprusside (SNP) but significantly potentiated the relaxant capacity of the PDE5 inhibitor tadalafil (pEC₅₀ 4.40±0.03 vs. 5.43±0.29, p

Citation: Sevilleja-Ortiz, Alejandro; Fernández, Argentina; El Assar, Mariam; García-Rojo, Esther; García-Gómez, Borja; La Fuente, José María; Romero-Otero, Javier; Rodríguez-Mañas, Leocadio; Angulo, Javier (2021) Diabetes is associated with functional alterations in rat and human penile vascular tissue through Orai channels. Proceedings of the VI Congreso de Señalización Celular, SECUAH 2021. 29 de marzo a 30 de abril, 2021. Universidad de Alcalá. Alcalá de Henares, Madrid. España. *dianas* 10 (1): e202103b06. ISSN 1886-8746 (electronic) *journal.dianas*. e202103b06 <http://www3.uah.es/dianas?e202103b06>. URI <http://hdl.handle.net/10017/15181>

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