MCB, vol.16, supplemental 2, pp.140-141, 2019

Endothelial Tight Junction Protein ZO-1 Response to Multiple-Mechanical Stimulations After Stent Implamtation

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Abstract: Zonula occludens-1 (ZO-1) is a peripheral membrane protein belongs to the family of zona occludens proteins and plays an important role as a scaffold protein which cross-links and anchors tight junction (TJ) strand proteins, within the lipid bilayer, to the actin cytoskeleton [1-2]. Stent implantation is the most effective method in the treatment of cardiovascular disease which always destroy junctions of endothelial cells, the functions of the tight junction were also affected. However, the role of ZO-1 before and after stent implantation has not been fully understood. In this study, the expression of ZO-1 were analyzed by qPCR, western blot and immunofluorescence *in vivo* and *in vitro*. *In vivo* experiments were developed in two animal modes, carotid ligation of ApoE$^{-/-}$ mice for 48 h and abdominal aorta poly (L-lactic acid) stents implantation of male SD rats for indicated time (1 week, 1 month, 3 month and 1 year). *In vitro*, HUVECs were exposed to fluid shear stress and static pressure respectively. Namely, shear stress at 5 dyn/cm^2 (low shear stress, LSS) and 12 dyn/cm^2 (high shear stress) for 6 h, and 40 kPa static pressure for 6 h and 12 h. *In vivo*, expression of ZO-1 showed interestingly lower, compared to control in ApoE$^{-/-}$ mice and SD rats, except stents implantation at 3 month. *In vitro*, the expression level of ZO-1 showed higher at indicated shear stress, no statistical difference under static pressure at 6 h but significantly higher at 12 h, compared to control. Fluorescent staining showed more loose connection between cells and surrounding edges of the cells presented a gear shape with many small forks. In conclusion, we tried to indicate the role of ZO-1 before and after stent implantation by applying different mechanical stimulations respectively to imitate the mechanical environment endothelial cells might confront *in vivo*. Interestingly, we found that expression of ZO-1 was diametrically opposed *in vitro* and *in vivo* except stents implantation for 3 month in rats. Overall, our research revealed that ZO-1 response to multiple-mechanical stimulations, and ZO-1 might be inhibited or degraded in RNA level for multiplex mechanical stimulations *in vivo*, which shall pave the way for further research.

Keywords: ZO-1; tight junction; stent implantation; mechanical stimulation

DOI: 10.32604/mcb.2019.07300

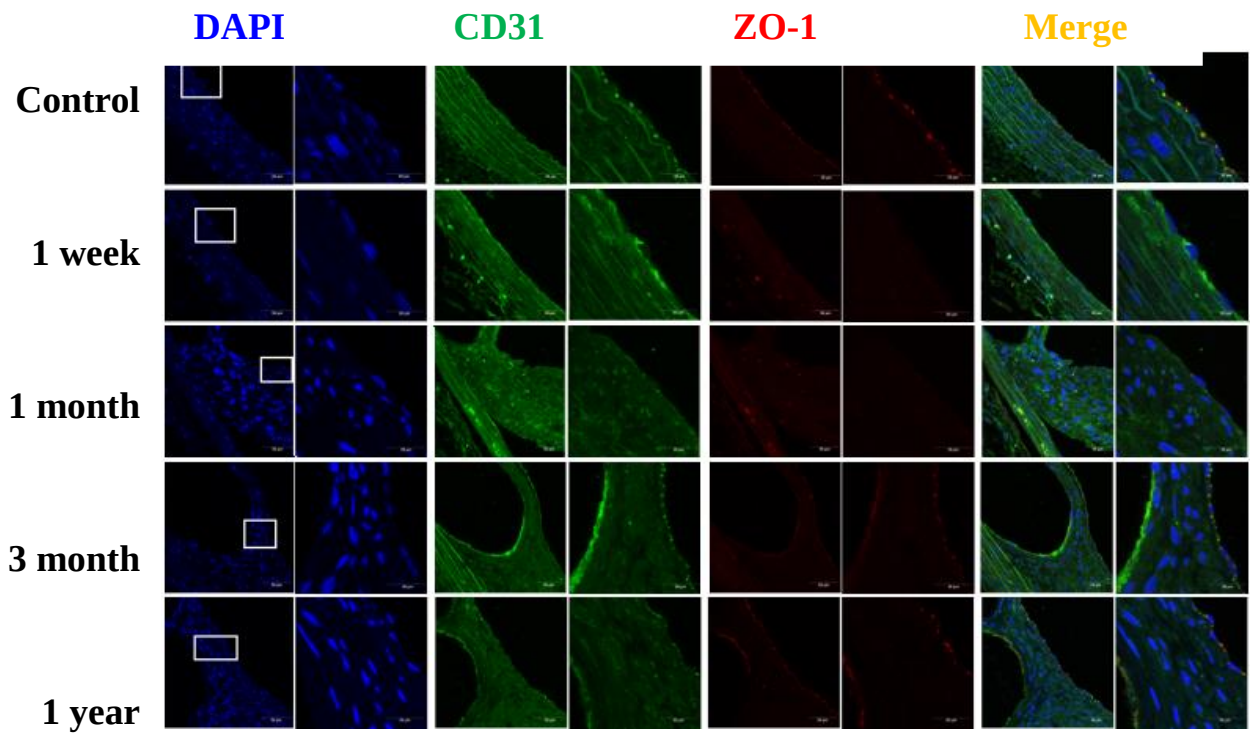

Figure 1. Expression of ZO-1 in SD rats post-implantation at indicated time

Acknowledgement: This study is supported by the National Science Foundation of China (nos: 11572064, 11332003, and 31701275), the National Key R&D Program of China (2016YFC1102305), the Fundamental Research Funds for the Central Universities (106112018CDPTCG0001-1 and 2019CDXYSG0004).

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