Laszlo Deres et al., J Clin Exp Cardiology 2018, Volume 9
DOI: 10.4172/2155-9880-C2-093

Effect of PARP-1 inhibition on the mitochondrial fragmentation in an *in vivo* SHR model

Laszlo Deres[1,2,3], **Krisztian Eros**[1,2,3], **Orsolya Horvath**[1], **Katalin Ordog**[1], **Kalman Toth**[1,2,3] and **Robert Halmosi**[1,2,3]
[1]University of Pecs, Hungary
[2]Szentagothai Research Center, Hungary
[3]MTA-PTE Working Group on Nuclear and Mitochondrial Function, Hungary

Introduction: Mitochondria form a highly dynamic network, which current state is determined by fusion-fission processes. Oxidative stress induced fragmentation of cardiac mitochondria is a well known phenomenon, which has profound effects on cell viability. Thus, influencing these processes may have therapeutic importance. In our experiment, we evaluated the effect of PARP-1 inhibition on cardiac mitochondrial changes due to persistent hypertension.

Methods: 10 weeks old male SHR rats received 5 mg/kg/day L-2286 PARP-1 inhibitor (SHR-L) or placebo (SHR-C) treatment for 32 weeks. Normotensive controls were male Wistar rats (WKY). After the treatment, electron microscopic preparations were made from cardiac tissues. We evaluated the average areas of inter-fibrillar mitochondria (IFM) on longitudinal sections. The levels of proteins involved in mitochondrial dynamics (the pro-fission Drp1 GTPase and cristae membrane integrity influencing Opa1) were monitored by fractioned Western blot samples.

Results: Mitochondria showed greater heterogeneity in both shape and size in the SHR-C group, and dilatation of cristae spaces were observed. These alterations were less pronounced in the treatment group. We found increased fragmentation of mitochondria in the SHR-C group ($p<0.05$ vs. WKY), which was significantly attenuated by the L-2286 treatment. Western blot analysis showed decreased translocation of the pro-fission Drp1 protein into the mitochondria in the SHR-L group compared to the SHR-C group. No significant changes were observed in the level of Opa1 expression.

Discussion: In a hypertensive animal model, the oxidative stress-induced cardiac mitochondrial fragmentation was significantly attenuated by L-2286 treatment. This may be due to the favorable signaling effect of PARP-1 inhibition beside its well-known effect on increased oxidative stress resistance and on increased bioenergetic stability of the heart.

Biography

Laszlo Deres has completed his PhD in 2015 at the University of Pecs Medical School. He is a member of the Genomic and Experimental Cardiology Research Group taking place at the Szentágothai Research Center, University of Pecs.

deres.laszlo@pte.hu

Notes: