

JOINT EVENT

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Involvement of Nrf2 transcriptional activity in the induction of HO1 in abdominal aortic aneurysm wall of simvastatin treated patientsAleksandra Piechota-Polanczyk¹, Aleksandra Kopacz¹, Damian Kloska¹, Anna Grochot-Przeczek¹, Ihor Huk³ and Alicja Jozkowicz¹¹Jagiellonian University, Poland²University of Agriculture in Krakow, Poland³Medical University of Vienna, Austria

Statement of the Problem: Lack of Nrf2-regulated antioxidative heme oxygenase-1 (HO-1) may exacerbate abdominal aortic aneurysm (AAA). However, the effect of simvastatin on Nrf2/HO-1 pathway in patients with AAA has not been studied yet.

Methodology & Theoretical Orientation: We analyzed the localization of Nrf2 and HO-1 in human AAA wall and verified the influence of simvastatin treatment on Nrf2. We took AAA tissue from patients treated with simvastatin (N=28) or without statins (N=14) and verified the effect of simvastatin on primary human aortic endothelial (EC) and smooth muscle cells (SMC).

Findings: We found a positive correlation between expression of gene and glutathione (GSH) in AAA wall. Both, *HMOX-1* and GSH are regulated by Nrf2. However, the expression of Nrf2 and HO-1 seemed not to colocalize in AAA wall. Simvastatin treatment up-regulated HO-1 in AAA, but Nrf2 level was only higher in vasa vasorum. *In vitro* studies showed that simvastatin raises HO-1 protein in EC and SMC but independently on NFE2L2.

Conclusion & Significance: Simvastatin-induced modulation of HO-1 in ECs and SMCs *in vitro* is not related to Nrf2/ARE activity. Different HO-1 and Nrf2 localization together with stable expression of Nrf2 target genes in AAA tissue signify Nrf2-independency.

Recent Publications

1. Loboda (2017) Role of Nrf2/HO-1 system in development, oxidative stress response and diseases: an evolutionarily conserved mechanism. *Cellular and Molecular Life Sciences* 73(17): 3221-47.
2. Rodella (2016) Abdominal aortic aneurysm and histological, clinical, radiological correlation. *Acta Histochemica* 118(3):256-62.
3. Piechota-Polanczyk and Jozkowicz (2016) The role of statins in heme oxygenase-1 activation in cardiovascular diseases. *Current Drug Targets* 18(6): 674-686.
4. Pantan (2016) Synergistic effect of atorvastatin and Cyanidin-3-glucoside on angiotensin II-induced inflammation in vascular smooth muscle cells. *Experimental Cell Research* 342(25):104-112.
5. Jez M (2017) Valproic acid downregulates heme oxygenase-1 independently of Nrf2 by increasing ubiquitination and proteasomal degradation. *Biochemical and Biophysical Research Communications* 485(8):160-166.

Biography

Aleksandra Piechota-Polanczyk is currently employed as an Associate Professor at the Department of Medical Biotechnology, Jagiellonian University in the frame of the project entitled: Role of heme oxygenase 1 in the development and progression of abdominal aortic aneurysm. She received her PhD in Medicine with specialty of Medical Biology in 2011. She was a Leading Researcher in Professor Ihor Huk research group (VASLAB) at the Medical University of Vienna, Austria with whom she is now cooperating. Her research interests focuses on finding of new anti-oxidative and anti-inflammatory proteins that could be potential markers and/or targets in treatment of gastrointestinal and cardiovascular diseases, as well as the role of Nrf2 and heme oxygenase 1 in cellular adaptation to oxidative stress and inflammatory reactions.