The 7th World Congress on
Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)
Sorrento, Italy April 11-13, 2019
www.codhy.com codhy@codhy.com

INDUCTION OF HISTONE DEACETYLASE SIGNALING PATHWAYS AUGMENTS VASCULAR INFLAMMATION AND REMODELING IN DIABETIC MICE

S.A. Manea, A.-G. Lazar, M.-L. Vlad, M. T. Cosac, A. Manea
Molecular and Cellular Pharmacology - Functional Genomics Laboratory, Institute of Cellular Biology and Pathology "Nicolae Simionescu", Romania

Purpose: Up-regulation of pro-inflammatory molecules and enhanced synthesis of extracellular matrix proteins induces structural and functional alterations of the blood vessel wall in diabetes. The transcriptional control mechanisms of inflammation and vascular remodeling-related genes are not completely defined. Epigenetic alterations mediated by histone deacetylase (HDAC) may contribute to pathoetiology of diabetic vasculopathies. The aim of this study was to uncover the role of HDAC in regulating vascular inflammation and remodeling in diabetic mice. **Methods:** Male C57Bl/6J non-diabetic and streptozotocin-induced diabetic animals were distributed into three experimental groups to receive vehicle or SAHA (10 mg/kg, 4 weeks), a pan-HDAC inhibitor. Real time PCR, western blot, and microscopy were employed to investigate the regulation of various HDAC subtypes and markers of inflammation and vascular remodeling. **Results:** Class I (HDAC2, HDAC3), class II (HDAC4), and class IV (HDAC11) HDAC subtypes were found significantly elevated in the aorta of diabetic mice as compared to non-diabetic animals. The augmented expression of HDAC enzymes correlated with elevated levels of markers of vascular inflammation [big-endothelin-1 (bigET-1), inducible nitric oxide synthase (NOS2), matrix metalloproteinase (MMP) 9] and remodeling [MMP2, MMP9, fibronectin (FN), laminin (LM)]. Treatment of diabetic mice with SAHA significantly reduced the aortic expression of bigET-1, NOS2, MMP2, MMP9, FN, and LM. **Conclusions:** Induction of inflammation- and remodeling-related molecules is mediated by up-regulated HDAC in the aorta of diabetic mice. Pharmacological targeting of HDAC may represent an important therapeutic strategy in diabetes-associated cardiovascular disorders. **Financial Disclosure:** No **Acknowledgements:** Work supported by UEFISCDI (PN-III-P4-ID-PCE-2016-0665, PN-III-P1-1.1-TE-2016-0851).