Subrata Chakrabarti, J Diabetes Metab 2014, 5:10
http://dx.doi.org/10.4172/2155-6156.S1.026

OMICS Group Conferences
Accelerating Scientific Discovery

5th World Congress on
Diabetes & Metabolism
November 03-05, 2014 Embassy Suites Las Vegas, USA

Chronic diabetic complications: An accelerated aging process resulting from DNA damage and epigenetic alterations

Subrata Chakrabarti
Western University, Canada

Chronic diabetic complications are major causes of mortality and morbidity. Hyperglycemia activates several signaling pathways producing oxidative stress. These pathways converge on the nucleus causing DNA damage and changes in the transcription machinery of endothelial cells. Such process is further regulated post-transcriptionally by small, non-protein coding microRNAs. The cells and tissues ultimately develop an aging-like phenotype with impaired function. DNA damage activates nucleotide excision repair enzymes, including ERCC1, ERCC4 and PARP. In addition, augmented production of histone acetylator P300 and alterations of several histone deacetylases including class III deacetylase, sirtuins (SIRTs) occur. There are also extensive interactions and interregulations among these molecules. In this study, we examined three different endothelial cells and tissues from diabetic animals and human and found that such above mentioned processes cause activation of several transcription factors; subsequently resulting in increased transcription of multiple vasoactive factors and extracellular matrix proteins. The list includes collagen, fibronectin, TGFβ1, endothelin 1, vascular endothelial growth factor etc. Here we show alterations of specific miRNAs, namely miR200b, miR146a and miR195 regulating vascular endothelial growth factor, fibronectin and SIRT1 respectively. Furthermore, we have demonstrated relationship of specific miRNA production with p300 and histone acetylation. Detailed study further revealed that, through these mechanisms, hyperglycemia causes accelerated aging-like changes in the endothelial cells and in the tissues affected by chronic diabetic complications such as retina, kidney and the heart. Exploration of such mechanisms has potentially identified novel treatment options for chronic diabetic complications using microRNAs and targeting epigenetic mechanisms.

Biography

Subrata Chakrabarti received MBBS from Calcutta University in India. He received MSc and PhD and completed residency training at the University of Manitoba. He received FRCP(C) in Anatomical Pathology. Following completion of a fellowship from Yale University, he joined Western University in 1994. His research focuses on chronic diabetic complications. He has published more than 170 peer-reviewed articles and a large number of review articles and book chapters. He is currently Chair, Dept. of Pathology at Western University and Chief of pathology and laboratory Medicine at London Health Sciences Centre & St. Joseph's Health Care, London, Ontario, Canada.

Subrata.Chakrabarti@schulich.uwo.ca