OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Diabetes & Metabolism
August 14-16, 2013 Holiday Inn Chicago-North Shore, IL, USA

Identification of a novel -99A>T IAPP gene mutation in a north Indian type II diabetes patient with hypertension

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Aim: Several studies conducted worldwide supports that mutations in activator domains of promoter region (-91 to -222 bp) of *IAPP* gene can lead to increased Islet amyloid deposition, ß cells destruction and insulin resistance. Considering it a pilot study was conducted to identify amylin promoter mutation and its association in patients diagnosed having both type-2-diabetes and hypertension.

Methods: Fifty Hypertensive type-2-diabetic individuals who are free from any micro-vascular complications, in order to exclude nephropathy induced hypertension and 50 healthy controls were included in our study. Genomic DNA of these individuals were isolated from whole blood, proximal promoter of the amylin gene including 207 bp upstream of TATA box was amplified by PCR, and subject to SSCP analysis. Samples with mobility shifts were selected for genotyping by DNA sequencing.

Results: Strikingly we identified a novel −99A>T mutation in a 35 year old female patient with BMI of 26.4 kg/m² and family history of diabetes and hypertension. To elucidate whether the identified mutation disrupts the binding site for transcription factors, potential binding sites in the vicinity of this mutation was screened for using the TESS master (*Transcription Element Search System*) a computer program on TRANSFAC, EMBL, CBIL databases. This −99A>T mutation produced a sequence 5'-ATTGG-3' (corresponding to −101 to −97 of IAPP gene promoter) and its complementary sequence 3'-TAACC-5' formed a putative binding site for CAAT box binding transcription factors (CTF) like CBP, CP-1, C/EBPα. All these CTFs are well established transcription activators, their role in initiation and maintaining efficiency of eukaryotic transcription is also very well established.

Conclusion: This activator domain −99A>T mutation of *IAPP* gene can possibly increase gene transcription, production, deposition of Islet amyloid ultimately leading to pathogenesis of type-2-diabetes.

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