

ABSTRACTS

Role of sestrin2 in the regulation of ER stress and pro-inflammation under diabetes with dyslipidemia

Sundararajan S, Jayachandran I, Venkatesan S, Balasubramanyam M, Mohan V, Venkatesan B, Manickam N

Madras Diabetes Research Foundation, Chennai, India

Abstract

Introduction: Diabetes is a group of metabolic disorders characterized by hyperglycemia and associated chronic complications including cardiovascular diseases. Hyperglycemia induces various stress conditions including oxidative /endoplasmic reticulum (ER) stress, leading to inflammatory disorders in vascular system. Sestrin2, an antioxidant, is involved in the glucose and lipid homeostasis by regulating mTOR activity. However, the roles of sestrin2 in the regulation of ER stress and pro-inflammation in diabetic patients remains unclear. Hence, the present study is focused on evaluating the status of sestrin2 and its effect on ER stress and pro-inflammation in the diabetic dyslipidemia.

Methods: Human subjects with diabetes and/or dyslipidemia were recruited to study the status of sestrin2, ER stress markers, and pro-inflammatory markers in peripheral mononuclear cells (PBMC) and monocytes. Human monocytic cell line (THP1) was over expressed with sestrin2 and treated with high glucose and then analyzed the expression levels of oxidative stress, ER stress and pro-inflammatory markers.

Observations: The expressions of ER stress/pro-inflammatory markers were significantly increased in the PBMC of patients with diabetes or dyslipidemia, and those with both the conditions. Sestrin2 expression was also significantly reduced in the monocytes of persons with metabolic disorder. In *in vitro* conditions, high glucose induction increased the expression levels of ER stress, oxidative stress, pro-inflammatory markers and decreased the sestrin2 levels. Sestrin2 overexpression reverted all the ill effects of high glucose in THP1 cells.

Conclusion: Sestrin2 is involved in the regulation of pro-inflammation, ER stress and oxidative stress in diabetes condition.

Keywords: Sestrin2, pro-inflammation, ER stress, oxidative stress, diabetes, dyslipidemia

Presented on: 13 October 2019

Presented by: Saravanakumar Sundararajan