

## Protective Role of Autophagy Challenging the Stresses of Type 2 Diabetes and Dyslipidemia

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**Abstract :** The global challenge of type 2 diabetes mellitus is a major health concern in this millennium, and researchers are continuously exploring new targets to develop a novel therapeutic strategy. Type 2 diabetes mellitus (T2DM) is often coupled with dyslipidemia increasing the risks for cardiovascular (CVD) complications. Enhanced oxidative and nitrosative stresses appear to be the major risk factors underlying insulin resistance, dyslipidemia,  $\beta$ -cell dysfunction, and T2DM pathogenesis. Autophagy emerges to be a promising defense mechanism against stress-mediated cell damage regulating tissue homeostasis, cellular quality control, and energy production, promoting cell survival. In this study, we have attempted to explore the pivotal role of autophagy in T2DM subjects with or without dyslipidemia in peripheral blood mononuclear cells and insulin-resistant HepG2 cells utilizing flow cytometric platform, confocal microscopy, and molecular biology techniques like western blotting, immunofluorescence, and real-time polymerase chain reaction. In the case of T2DM with dyslipidemia higher population of autophagy, positive cells were detected compared to patients with the only T2DM, which might have resulted due to higher stress. Autophagy was observed to be triggered both by oxidative and nitrosative stress revealing a novel finding of our research. LC3 puncta was observed in peripheral blood mononuclear cells and periphery of HepG2 cells in the case of the diabetic and diabetic-dyslipidemic conditions. Increased expression of ATG5, LC3B, and Beclin supports the autophagic pathway in both PBMC and insulin-resistant Hep G2 cells. Upon blocking autophagy by 3-methyl adenine (3MA), the apoptotic cell population increased significantly, as observed by caspase-3 cleavage and reduced expression of Bcl2. Autophagy has also been evidenced to control oxidative stress-mediated up-regulation of inflammatory markers like IL-6 and TNF- $\alpha$ . To conclude, this study elucidates autophagy to play a protective role in the case of diabetes mellitus with dyslipidemia. In the present scenario, this study demands to have a significant impact on developing a new therapeutic strategy for diabetic dyslipidemic subjects by enhancing autophagic activity.

**Keywords :** autophagy, apoptosis, dyslipidemia, reactive oxygen species, reactive nitrogen species, Type 2 diabetes

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