Unveiling the Methylglyoxal contribution to β-cell failure and glucose intolerance in Glo1KD mice

Nigro Cecilia[1], Leone Alessia[1], Nicolò Antonella[1], Prevenzano Immacolata[2], D'Esposito Vittoria[1], Conza Domenico[1], Pirozzi Marinella[1], Parashuraman Raman[1], Colanzi Antonino[1], Miele Claudia[1].

[1]Istituto per l'Endocrinologia e l'Oncologia Sperimentale (IEOS)/CNR; [2]Dipartimento di Scienze Mediche Traslazionali (DiSMeT), Università degli Studi di Napoli "Federico II".

Background: (max 50 words)

Exogenous exposure or endogenous accumulation due to metabolic pathway imbalances leads to Methylglyoxal accumulation, which induces the formation of advanced glycation end products, causing cellular dysfunction. Evidence demonstrates the role of Methylglyoxal in the progression of diabetes complications.

Our aim is to uncover the molecular determinants of Methylglyoxal-induced defects in pancreatic islets.

Methods and Results: (max 100 words)

mRNA sequencing was performed on islets isolated from a transgenic mouse model (Glo1KD), developing elevated Methylglyoxal and glucose intolerance. Transcriptome analysis of Glo1KD vs. WT islets revealed differential expression of 761 genes, including 11 related to mitochondrial function, crucial for insulin secretion. The top 30 differentially expressed genes included four members of the regenerating islet-derived (Reg) gene family, playing protective roles against β-cell damage caused by drugs or environmental factors. Reg gene downregulation was confirmed *in vitro* in a Methylglyoxal-exposed pancreatic β-cell line. Prediction analysis for transcription factors binding to Reg gene promoters indicated STAT1 as a potential shared regulator.

Conclusions and Significance: (max 50 words)

This study reveals a link between the Methylglyoxal-dependent impairment of islets homeostasis and Reg genes downregulation. Ongoing investigations using cell imaging and analysis of the molecular aspects of Methylglyoxal-induced cellular impairment will help identify targetable pathways for novel treatments aimed at restoring β-cell function and preventing or delaying diabetes progression.

Keywords: (max 5)

Glycation, Transcriptional regulation, Type 2 Diabetes Mellitus, β-cell function.

References: (max 5 relevant references from the Authors in the following format:

full authors list, *title*, *year*, *journal*, *vol.: pages*)

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