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Quantitative Analysis of Orphan Nuclear Receptors in Insulin Resistant C2C12 Skeletal Muscle Cells

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Abstract : Nuclear Receptors (NR) are a super family of transcription factors that play a major role in lipid and glucose metabolism in skeletal muscle. Recently, pharmacological evidence supports the view that stimulation of nuclear receptors alleviates Type 2 Diabetes (T2D). The orphan nuclear receptors (ONR) are members of the nuclear receptor (NR) superfamily whose ligands and physiological functions remain unknown. To date, no systematic studies have been carried out to screen for ONRs expressed in insulin resistant (IR) skeletal muscle cells. Therefore, in this study, we have established a model for IR by treating C2C12 skeletal muscle cells with insulin (10nM) for 48 hours. Western Blot analysis of phosphorylated AKT confirmed IR. Real-time quantitative polymerase chain reaction (qPCR) results highlighted key ONRs including NUR77 (NR4A1), NURR1 (NR4A2) and NOR1 (NR4A3) which have been associated with fatty acid oxidation regulation and glucose homeostasis. Increased mRNA expression levels of estrogen-related receptors (ERRs), REV-ERBα, NUR77, NURR1, NOR1, in insulin resistant C2C12 skeletal muscle cells, indicated that these ONRs could potentially play a pivotal regulatory role of insulin secretion in lipid metabolism. Taken together, this study has successfully contributed to the complete analysis of ONR in IR, and has filled in an important void in the study and treatment of T2D.

Keywords : type 2 diabetes, orphan nuclear receptors, transcription receptors, quantitative mRNA expression
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