Role of TMEM-143 in Glucose Homeostasis-Implications in the Pathogenesis of Type-2 Diabetes

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TMEM-143 (Transmembrane protein 143) human gene is located in the Chr19q13.33 chromosomal region, which is known to be associated with the risk of type-2 diabetes and cancer. TMEM-143 gene is translated into a protein of unknown function, predicted to contain a mitochondrial signal sequence, and to reside as an integral membrane protein (dual-pass protein) in the mitochondria. Screening of normal human tissues by RT-PCR revealed a high expression of the TMEM-143 gene in metabolic tissues such as the skeletal muscle tissue (data not shown). In this study, we sought to elucidate the TMEM-143 expression pattern, subcellular localization, and function in myoblasts C2C12 and pre-adipocytes 3T3-L1. RT-PCR and western blot revealed that TMEM-143 expression increased during the differentiation process of 3T3 and C2C12 into adipocytes and myotubes respectively. We found that TMEM-143 expression level can be modulated by anti-diabetic drugs such as Insulin, Rosiglitazone, and Metformin. Confocal fluorescence imaging (CFI) revealed that TMEM-143 is localized in mitochondria, plasma membrane, and nucleus. Furthermore, CFI uncovered that TMEM-143 co-localized with glucose transporter type 4 (GLUT-4). TMEM-143 silencing with siRNA did not induce mitochondrial dysfunction (cell death) but induced a decrease in both GLUT-4 and PAKT levels, suggesting that the GLUT-4 associated AKT-dependent signaling pathway was affected. Subsequently, the glucose uptake by 3T3 or C2C12 was significantly inhibited by more than 50%. TMEM-143 may play a physiological role in glucose homeostasis and merits further investigation.

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