Novel actin filaments regulate glucose clearance, insulin sensitivity and insulin secretion

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The onset of Type 2 diabetes is associated with alterations in both glucose uptake and insulin secretion. Glucose uptake involves a shift of Glut-4 vesicles from intracellular stores to the cell surface, whilst insulin secretion involves the fusion of insulin-containing granules with the pancreatic β-cell surface. We have identified novel actin cytoskeletons defined by the cytoskeletal tropomyosin (Tm) isoform Tm5NM1. Experimental analysis using Tm5NM1 transgenic (Tg) mice suggests these filaments play a role in both glucose uptake and basal insulin secretion. Tg mice have increased glucose clearance in part due to increased insulin sensitivity. The molecular events facilitating Glut4 translocation include activation of the PI3-kinase pathway and also major rearrangements of cytoskeleton components. Tm5NM1 Tg mice showed no change in insulin-stimulated Akt phosphorylation suggesting Tm5NM1 is acting downstream of insulin signalling. Using gene expression profiling with a dedicated microarray, an increase in genes involved in GLUT4 trafficking and actin filament turnover was detected in adipose tissue from Tg mice. The gene expression of genes involved in Glut-4 trafficking was examined by quantitative real-time PCR analysis (n=10/gp). Two genes Myo1c and Sec8 were increased in Tg adipose tissue ($P<0.05$ and $P<0.005$ respectively), Myolc and Sec8 were also increased at the protein level (Western blot). We propose that Tm5NM1 induces more stable cortical actin filament network in adipocytes leading to the accumulation of GLUT4 trafficking machinery and enhancing glucose uptake.