
Abstract
Evidence suggests that chromium supplementation may alleviate symptoms associated with diabetes, such as high blood glucose and lipid abnormalities, yet a molecular mechanism remains unclear. Here, we report that trivalent chromium in the chloride (CrCl₃) or picolinate (CrPic) salt forms mobilize the glucose transporter, GLUT4, to the plasma membrane in 3T3-L1 adipocytes. Concomitant with an increase in GLUT4 at the plasma membrane, insulin-stimulated glucose transport was enhanced by chromium treatment. In contrast, the chromium-mobilized pool of transporters was not active in the absence of insulin. Microscopic analysis of an exofacially Myc-tagged enhanced green fluorescent protein-GLUT4 construct revealed that the chromium-induced accumulation of GLUT4-containing vesicles occurred adjacent to the inner cell surface membrane. With insulin these transporters physically incorporated into the plasma membrane. Regulation of GLUT4 translocation by chromium did not involve known insulin signaling proteins such as the insulin receptor, insulin receptor substrate-1, phosphatidylinositol 3-kinase, and Akt. Consistent with a reported effect of chromium on increasing membrane fluidity, we found that chromium treatment decreased plasma membrane cholesterol. Interestingly, cholesterol add-back to the plasma membrane prevented the beneficial effect of chromium on both GLUT4 mobilization and insulin-stimulated glucose transport. Furthermore, chromium action was absent in methyl-beta-cyclodextrin-pretreated cells already displaying reduced plasma membrane cholesterol and increased GLUT4 translocation. Together, these data reveal a novel mechanism by which chromium may enhance GLUT4 trafficking and insulin-stimulated glucose transport. Moreover, these findings at the level of the cell are consistent with in vivo observations of improved glucose tolerance and decreased circulating cholesterol levels after chromium supplementation.