Skeletal muscle glucose uptake is increased by exercise. The increased uptake is a function of both an increase in muscle glucose extraction and in muscle blood flow. The latter is quantitatively the most important factor since muscle blood flow may increase up to 20 fold whereas glucose extraction only increases 2-3-(4) fold (Richter, 1996). The contraction-induced increase in glucose transport is in large measure due to translocation of GLUT4 to the surface membrane as indicated by the almost total absence of contraction-induced muscle glucose transport in GLUT4 knockout mice (Zisman et al., 2000). GLUT4 is expressed in a muscle fiber type specific manner. Yet, in human quadriceps muscle the difference in GLUT4 expression between type I and type II fibers is only in the order of 20% (Daugaard et al., 2000) which is much less than in rat skeletal muscle. Physical training increases muscle GLUT4 expression but decreases muscle glucose utilization during submaximal exercise. We have recently shown that this is due to a decreased translocation of GLUT4 to the surface membrane in trained muscle (Richter et al., 1998). However, if exercise is carried out at a high relative work load (80-100% of peak VO_{2max}) glucose uptake is in fact increased in trained muscle. Furthermore, the increase seems to be dependent on the training-induced increase in muscle GLUT4 protein expression (Kristiansen et al., 2000). Contraction-induced muscle glucose transport and GLUT4 translocation is dependent on the pre-contraction muscle glycogen concentration, however only in fast-twitch fibers (Derave et al., 1999). The exact mechanism behind this effect of glycogen is unknown but may be related to glycogen dependent activation of 5`AMP-kinase. However, recently we have described that in contracting rat slow-twitch muscle activation of AMPK is dissociated from activation of glucose transport (Derave et al., 2000). AMPK is activated in an intensity and isoform specific manner in human skeletal muscle during exercise (Wojtaszewski et al., 2000). Its role in regulation of muscle glucose uptake is, however, still unclear.