Serum- and Glucocorticoid-Inducible Kinase 1 (SGK1) Regulates Adipocyte Differentiation via Forkhead Box O1

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The serum and glucocorticoid-inducible kinase 1 (SGK1) is an inducible kinase the physiological function of which has been characterized primarily in the kidney. Here we show that SGK1 is expressed in white adipose tissue and that its levels are induced in the conversion of preadipocytes into fat cells. Adipocyte differentiation is significantly diminished via small interfering RNA inhibition of endogenous SGK1 expression, whereas ectopic expression of SGK1 in mesenchymal precursor cells promotes adipogenesis. The SGK1-mediated phenotypic effects on differentiation parallel changes in themRNA levels for critical regulators and markers of adipogenesis, such as peroxisome proliferator-activated receptor _, CCAAT enhancer binding protein _, and fatty acid binding protein aP2. We demonstrate that SGK1 affects differentiation by direct phosphorylation of Foxo1, thereby changing its cellular localization from the nucleus to the cytosol. In addition we show that SGK1_/_cells are unable to relocalize Foxo1 to the cytosol in response to dexamethasone. Together these results show that SGK1 influences adipocyte differentiation by regulating Foxo1 phosphorylation and reveal a potentially important function for this kinase in the control of fat mass and function. **(*Molecular Endocrinology* 24: 370–380, 2010)**