Introduction: Renal hypertrophy, extracellular matrix accumulation, aItered apoptosis as well as changes in regional hemodynamics have been implicated in the pathophysiology of nephropathy in diabetes mellitus (DM). On the molecular level the detailed mechanisms for development of diabetic nephropathy (DN) have becn intensively studied. Insulin induces a variety of biologicaI effects in a number of cell types via phosphatidylinositol-3 kinase (PI3K)/Akt kinase signaling pathway. Considering multiple function of Akt that incIude potentiaIly hannful pro-growth effects mediated by mTOR and cyclooxygenas-2 (COX-2), as well as protective effects mediated by endotheliaI nitric oxide synthase (eNOS), it is possible that aIterations in activities of Akt may play role in the pathophysiology ofDN.
Renal corticaI activity and expression of Akt, its down-strearn effectors mTOR, eNOS, and "C<JIX-:Z. as well as PTEN, an endogenous Akt inhibitor, were investigated in streptozotocin (STZ): diabetic rats as a model of Type 1 DM with different levels of glycenůc control, and in Zucker ~d.iabetic fatty rats, a model ofDM2, and in nondiabetic rats as controls.
Methods: Akt activity was measured by kinase assay. Protein expressions were measured by .immunoblotting and immunohistochemistry in renal cortex of 4- and 12- week old Zucker rats (ZDF), and lean controls (ZL). STZ rats were treated with various doses of exogenous insulin per day (OU, . 4U, 12U of insulin) to obtain different levels of metabolic control (STZO, STZ4, STZI2). The ·nneasnr<ml€mts were made 4 weeks after induction of DM, and results were compared with age matched non-diabetic control rats (K).
Results: PhysicaI and metabolic parameters in aIl groups of STZ and control rats retlected differences in metabolic control.