

Mechanism of cell apoptosis in Diabetic Nephropathy

Samy L Habib

Department of Cellular & Structural Biology and Geriatric Research, Education and Clinical Center South Texas Veterans Health Care System, USA

Apoptosis contributes to the development of diabetic nephropathy, but the mechanism by which high glucose (HG) induces apoptosis is not fully understood. Because the tuberin/mTOR pathway can modulate apoptosis, we studied the role of this pathway in apoptosis in type I diabetes and in cultured proximal tubular epithelial (PTE) cells exposed to HG. Compared with control rats, diabetic rats had more apoptotic cells in the kidney cortex. Induction of diabetes also increased phosphorylation of tuberin in association with mTOR activation (measured by p70S6K phosphorylation), inactivation of Bcl-2, increased cytosolic cytochrome c expression, activation of caspase 3, and cleavage of PARP; insulin treatment prevented these changes. In vitro, exposure of PTE cells to HG increased phosphorylation of tuberin and p70S6K, phosphorylation of Bcl-2, expression of cytosolic cytochrome c, and caspase 3 activity. High glucose induced translocation of the caspase substrate YY1 from the cytoplasm to the nucleus and enhanced cleavage of PARP. Pretreatment the cells with the mTOR inhibitor rapamycin reduced the number of apoptotic cells induced by HG and the downstream effects of mTOR activation noted above. Furthermore, gene silencing of tuberin with siRNA decreased cleavage of PARP. These data show that the tuberin/mTOR pathway promotes apoptosis of tubular epithelial cells in diabetes, mediated in part by cleavage of PARP by YY1.

Biography

Dr. Habib has completed his Ph.D at Roswell Park Cancer Center, Buffalo, NY and trained at University of California, Irvine, University of Texas, Austin, TX and University of Texas Health Science Center, San Antonio, TX. He has published more than 34 papers in reputed journals and serving as an editorial board member and Editor of 7 journals. Dr. Habib also holds the position as Research Scientist in the South Texas Veterans Health Care System at Audie Murphy VA Hospital. He was a recipient of several research grant awards from American Diabetes Association, American Heart Association, National Kidney Foundation, New Investigator Award and Merit Review Award from Veterans Affairs, and Pilot Research Award from NIH/NIDDK. He has recently received the Excellent of Performance Award from the VA. Dr. Habib has been a regular member of the Kidney Cancer Study Section of the Medical Research Program, Department of Defense.

Habib@uthscsa.edu