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# The role of endoplasmic reticulum stress in kidney disease

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Based on our current findings and the work of others we have generated the overall hypothesis that endoplasmic reticulum (ER) stress is a common feature and contributes to the development of kidney disease of diverse etiology. ER stress is caused by the accumulation of unfolded proteins in the endoplasmic reticulum. Many nephrotoxic drugs induce an ER stress response resulting in tubular damage causing acute kidney injury. We model this response in the C57BL/6 mouse using the nucleoside antibiotic tunicamycin (0.5 mg/kg, I.P.). We used this model to test the ability of a low molecular weight chemical chaperone, 4-phenylbutyrate (4-PBA), to inhibit ER stress-induced renal tubular injury. We found that treatment with 1g/kg/day 4-PBA significantly reduced the tubular injury score induced by tunicamycin and decreased the expression of the ER stress inducible pro-apoptotic gene CHOP/GADD153. Similarly, in vitro experiments demonstrated in human proximal tubular epithelial cells 4-PBA's inhibition of CHOP/GADD153 expression and apoptosis. Other work performed in the rat has shown that the ER stress response is associated with hypertension-induced proteinuria and interstitial renal fibrosis. 4-PBA treatment in these animals reduced 24-hour protein excretion and the percentage of PAS positive protein cast area. 4-PBA also reduced renal fibrosis as shown by reduced smooth muscle actin and collagen staining. Taken together, these results indicate that 4-PBA may provide an effective renal therapy for kidney injury associated with ER stress including that caused by nephrotoxic drugs and proteinuria.

## Biography

Dr. Dickhout received his PhD from McMaster University. He trained as a Postdoctoral Fellow with Dr. Allen W. Cowley Jr. in Physiology at the Medical College of Wisconsin. Dr. Dickhout was the inaugural holder of the Division of Nephrology Junior Researcher award. Dr. Dickhout is currently an Assistant Professor in the Department of Medicine, Division of Nephrology at McMaster University and St. Joseph's Healthcare Hamilton. Dr. Dickhout's research program is currently supported by the Canadian Institutes of Health Research. Dr. Dickhout has published over 25 peer-reviewed papers. The overall goal of Dr. Dickhout's research is to better understand the relationship between renal dysfunction and cardiovascular disease.

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