Evidence for Renal Lipid Accumulation, Impaired Mitochondrial Fatty Acid Oxidation and ER Stress in the Development of Renal Dysfunction Induced by Obesity

Authors
Shankar Munusamy, Jussara M do Carmo, Jonathan P Hosler, John E Hall

Institutions
Qatar University, Doha, Qatar
University of Mississippi Medical Center, Jackson, Missouri, USA

e mail
shankar.munusamy@qu.edu.qa

Obesity is a global epidemic and has been implicated as a risk factor for end-stage renal disease. In this study, we investigated the impact of obesity in the absence of hypertension, on renal lipid accumulation, oxidative stress, mitochondrial function, and endoplasmic reticulum (ER) stress, which could play a major role in the development of obesity-induced renal dysfunction. We compared two genetic mouse models of obesity which we have shown to be normotensive, the leptin-deficient ob/ob mice and a hyperleptinemic melanocortin 4 receptor knockout mice (LoxTB MC4R/-/-), to lean wild type (WT) C57BL/6J mice and littermate controls (WT-LoxTB) from LoxTB MC4R/-/- breeding colony respectively. We measured urinary albumin excretion, creatinine clearance, renal triglycerides, ATP levels, state-3 mitochondrial respiration, protein carbonylation (a marker of oxidative stress) and C/EBP homologous protein (CHOP) expression (a marker of ER stress) in these mice. Our results indicate that the ob/ob mice and LoxTB MC4R/-/- mice exhibit significant albuminuria, increased creatinine clearance (693±61.1 vs. 534±31.5 and 752.3±50.6 vs. 488.9±81.2 μL/min) and renal triglyceride accumulation (8.1±0.8 vs. 4.8±0.2 and 3.9±0.5 vs. 2.2±0.3 mg triglyceride/g tissue) expressed as ob/ob vs. WT and LoxTB MC4R/-/- vs. WT-LoxTB respectively. Despite significant decreases in renal ATP levels (6.0±0.3 vs. 7.9±0.4 and 5.0±0.2 vs. 8.1±1.1 pmol/ mg in both obese models, only the LoxTB MC4R/-/- mice kidneys showed an impaired state-3 fatty acid oxidation, increased protein carbonylation and 3-fold induction of CHOP protein compared to WT-LoxTB control mice. Taken together, our data suggest that obesity in the absence of hypertension cause only mild renal dysfunction, and unveils the potential involvement of oxidative stress, impaired fatty acid oxidation and ER stress in obesity-induced renal injury associated with MC4R deficiency.

ChIP-chip Investigation of Epigenetic Changes in Response to Various Glucose Environments

Authors
Yasmeen Salamah, Monaera Al-Jaber, Eman Al-Azwani, Eman Al-Odus, Binu George, Joel A. Malek

Institution
Weill Cornell Medical College in Qatar, Doha, Qatar

e mail
yas2005@qatar-med.cornell.edu

With the rise in incidences of Diabetes within the Middle East, it will be important to understand the environmental and genetic components of the disease. Epigenetic changes, including DNA methylation and Histone modifications, can be a response to environmental signals resulting in stable gene expression changes. To begin understanding the epigenetic effects of glucose in the diet we conducted Chromatin Immunoprecipitation followed by tiling array (ChIP-chip) analysis on in vitro cultures of cells grown in varying amounts of glucose. We have investigated the effects on DNA methylation and various Histone methylation levels. Results from this study are presented. Initial results from this study will guide more detailed analysis of the progress of epigenetic changes, their stability, and their possible transmission to future generations.