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## Cardiac, hepatic and renal complications in spontaneously developed diabetic nonhuman primates

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Obesity can lead to insulin resistant and type-2 diabetes mellitus (T2DM). Both obesity and diabetes are serious epidemic issues in developed and some developing countries. T2DM and obesity often complicate each other and escalate patients' other healthiness. Cardiac, hepatic and renal complications of diabetes and obesity have widely been reported and studied for decades. However, the underlying mechanisms and interactions between obesity and diabetes have yet to be elucidated further. Non-human primates (NHPs) can spontaneously develop obesity and diabetes which are the highly valuable models for research to delineate molecular and cellular mechanisms of their pathophysiology. In our housed dysglycemic and dyslipidemic cynomolgus monkeys we evaluated cardiac, hepatic and renal complications. Echocardiography in diabetic NHPs showed left ventricular systolic and diastolic dysfunctions accompanied with left atrial hypertrophic remodeling, the phenotypes similarly to those found in diabetic patients. In addition, dyslipidemic and diabetic monkeys can develop nonalcoholic fatty liver disease (NAFLD)/steatohepatitis (NASH) assembling to the human liver disease. We also evaluated diabetic nephropathy and its molecular mechanisms in diabetic NHPs with significantly high albuminuria. Transcriptome analysis of kidney biopsies showed differentially expressed genes (DEGs) with 75 DEGs related to diabetic nephropathy, but only one nephropathy specific gene (LCT lactase) and 4 other DEGs were highly altered in diabetic monkeys with albuminuria. Signaling pathway analysis of the relevant DEGs and encoded proteins highlighted the role of a kidney failure, renal and urological diseases and inflammatory diseases related network, in which the most pivotal gene in this network is tumor necrosis factor, indicating that nephropathy is a disease closely related to inflammation and cell death. Therefore, non-invasive echocardiography and quantitative biomarker measurements in NHP models can be powerful translational tools for evaluation of obesity and diabetes complications and for investigation of potential novel therapies due to the pathophysiological similarity between NHP and humans.

### Biography

Yong Fu Xiao is the Head of Pharmacology at Crown Bioscience, Inc. and Adjunct Professor of Rutgers University. He has extensive experiences in cardiovascular and metabolic research. He was an Assistant Professor of Medicine, Harvard University and Associate Biophysicist at Massachusetts General Hospital. Prior to joining Crown Bio, he was also a Principal Scientist and worked on gene and protein therapy for heart and metabolic diseases in Medtronic. He has published over 110 peer-reviewed papers, reviews, book chapters and granted over 6 patents.

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