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## High-fat, sucrose and salt-rich diet during rat spermatogenesis lead to the development of chronic kidney disease in the female offspring of the F2 generation

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Effects of feeding male rats during spermatogenesis a high-fat, high-sucrose and high-salt diet (HFSSD) over two generations (F0 and F1) on renal outcomes are unknown. Male F0 and F1 rats were fed either control diet (F0CD+F1CD) or HFSSD (F0HD+F1HD). The outcomes were glomerular filtration rate and urinary albumin excretion in F1 and F2 offspring. If both outcomes were altered a morphological and molecular assessment was done. F2 offspring of both sexes had a decreased GFR. However, increased urinary albumin excretion was only observed in female F2 F0HD+F1HD offspring compared with controls. F0HD+F1HD female F2 offspring developed glomerulosclerosis (+31%;  $p < .01$ ) and increased renal interstitial fibrosis (+52%;  $p < .05$ ). RNA sequencing followed by qRT-PCR validation showed that four genes (Enpp6, Tmem144, Cd300lf, and Actr3b) were differentially regulated in the kidneys of female F2 offspring. lncRNA XR-146683.1 expression decreased in female F0HD+F1HD F2 offspring and its expression was ( $r = 0.44$ ,  $p = .027$ ) correlated with the expression of Tmem144. Methylation of CpG islands in the promoter region of the Cd300lf gene was increased ( $p = .001$ ) in female F2 F0HD+F1HD offspring compared to controls. Promoter CpG island methylation rate of Cd300lf was inversely correlated with Cd300lf mRNA expression in F2 female offspring ( $r = -0.483$ ,  $p = .012$ ). Cd300lf mRNA expression was inversely correlated with the urinary albumin-to-creatinine ratio in female F2 offspring ( $r = -0.588$ ,  $p = .005$ ). Paternal pre-conceptual unhealthy diet given for two generations predispose female F2 offspring to chronic kidney disease due to epigenetic alterations of renal gene expression.

### Biography

Doctor Jian Li has long been engaged in basic and clinical research on reproductive medicine, cardiovascular and kidney diseases. Training 12 master degree students, 5 have graduated. Presided more than 10 funds including two national natural science fund. She had published more than 40 papers including paper in Neurosci Biobehav Rev, J Hypertens. FASEB J.

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