The Expression of two isoforms of Matrix Metalloproteinase-2 in aged mouse models of Diabetes Mellitus and Chronic Kidney Disease

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Objectives: The function of intracellular isoform of MMP-2 should be related to the tubular epithelial cell regulated necrosis especially in the murine model and there is much to be revealed in the various clinical conditions. This study was undertaken to explore the effects of ageing on kidneys in the backgrounds of diabetes and chronic kidney disease (CKD) using mouse models, and to compare the expressions of two isoforms of MMP-2, that is, secretory full length MMP-2 (FL-MMP-2) and intracellular N-terminal Truncated MMP-2 (NTT-MMP-2) in these models.

Methods: The two experimental murine models used were a streptozotocin (STZ)-induced Type I diabetes mellitus model and 5/6 nephrectomized (5/6Nx) murine model of CKD, both involved ICR mice. The abundance of two isoforms of MMP-2 was determined by qPCR and functional analyses were conducted. Moreover, the expressions of two isoforms of MMP-2 were determined semiquantitatively by immunohistochemical staining and we compared these with tissue damage.

Results: Both isoforms of MMP-2 were upregulated in the kidney tissues of the STZ-induced diabetic model and in the 5/6 nephrectomized (5/6Nx) model irrespective of age. Characteristically, NTT-MMP-2 expression in old control mice was elevated and in-line with qPCR results. In addition, its expression was limited to renal cortex, especially to the tubulointerstitial area rather than the glomerular area. In terms of tissue damage, tubulointerstitial fibrosis was more severe in old 5/6Nx mice than in their young counterparts, whereas glomerulosclerosis was comparable in old and young 5/6Nx mice.

Conclusions: The intracellular isoform of MMP-2 (NTT-MMP-2) was induced by ageing irrespective of the presence of diabetes mellitus or chronic kidney disease, and their induction may be related to tubulointerstitial fibrosis in chronic kidney disease.