GLOMERULAR DEPOSITION OF HOMOTRIMERIC TYPE I COLLAGEN IN THE COL1A2 DEFICIENT MOUSE

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ABSTRACT

In the novel type I collagen glomerulopathy identified in COL1A2 deficient mice (synthesize exclusively homotrimeric type I collagen) type I collagen accumulates in the renal mesangium. Under normal physiologic conditions, type I collagen is not present in the renal mesangium and accumulation is pathologic. The aims of this study were to 1) determine the natural progression of the glomerulopathy, 2) determine if the pathologic findings correlate with disease progression, and 3) to identify the mechanism responsible for glomerular collagen deposition. In both COL1A2 deficient and heterozygous animals the glomerulopathy begins postnatally, follows a pattern of glomerular maturation, appears progressive, exhibits a gene dose effect, and results in albuminuria in severely affected animals. Finally, based on quantitative RT-PCR of steady-state proα1(I) collagen mRNA levels and preliminary differential cleavage analyses of heterotrimeric and homotrimeric type I collagen by MMPs. We postulate that the mechanism responsible for the glomerular collagen deposition seen in COL1A2 deficient mice involves pretranslational mechanisms and aberrant degradation.