Analysis of ECM change at early time intervals of diabetic nephropathy

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Background: Diabetic nephropathy (DN) is a common underlying disease for patients receiving dialysis. Although dialysis is a therapy widely adopted now, it is time-consuming and causes patients' financial burden. In order to improve patients' QOL, to develop the novel therapeutic strategies for DN is indispensable. Extracellular matrix (ECM) modification has been noticed to occur to glomerular basement membrane (GBM) and its changes induced tissue pathogenesis. Here we focused on the investigation on glomerular-related ECM to elucidate the interaction between ECM and nephropathy on the DN progression.

Methods・Results・Discussion: The early stage DN model mice were established by injecting STZ (streptozocin) to mice. After 2 and 4 weeks, mice were dissected and kidneys were removed and subjected to further treatment for investigations on inflammatory damage and ECM change by HE, PAS, MT, immune staining and dot blot at time intervals. Mice injected with citric acid buffer were used as control. The results of histological experiments showed that ECM accumulation in glomeruli had already appeared at the early stage of DN progression. Moreover, the drastic accumulation of interstitial ECM and inflammatory ECM components, infiltration of macrophage, and its related factors were also observed in DN glomeruli. Furthermore, dot blot analysis revealed an increment of low molecules of main ECMs in GBM such as type IV collagen and laminin, while an increment of high molecules of interstitial ECM such as type I collagen and fibronectin which implies that the structural disruption of the main Glomerular basement ECM and fiber assembly of interstitial ECM in DN glomeruli.

Taken together, we suggest that the unordinary ECM accumulation might be due to the repeated processes of several kinds of ECM remodeling or reconstitution during DN progression.