Role of Laminin α1 in mesangial cell proliferation and mesangial matrix accumulation

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Laminin α1 (LAMA1), a subunit of the laminin-111 (LM-111) basement membrane component, has been implicated in various biological functions in vivo and in vitro. Since Lamα deletion cause early embryonic lethality, its roles in the kidney are unknown. We employed a conditional knockout mouse model with a deletion of Lamα in the epiblast lineage (LamαKO) to study the role of LAMA1 in kidney development and function. We found that adult LamαKO mice developed focal glomerulosclerosis and proteinuria with age. In addition, mesangial cell proliferation was increased, and the mesangial matrix, which normally contains LM-111, was significantly expanded. In vitro, mesangial cells from LamαKO mice exhibited significantly increased proliferation compared to those from controls. This increased proliferation was inhibited by the introduction of Lamα gene, suggesting a specific role for LAMA1 in regulating mesangial cell behavior. Moreover, TGF-β1-induced type IV collagen expression is increased in the absence of LAMA1, this increase was abrogated by transfection with the Lamα vector. These findings suggest that LAMA1 plays a critical role in kidney function and kidney aging by regulating the mesangial cell population and mesangial matrix deposition.