

Silencing of renal DNaseI is associated with up-regulation of tumor necrosis factor receptor-associated protein 1 (Trap1) during progression of murine and human lupus nephritis

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We have recently demonstrated that transformation of mild glomerulonephritis into end-stage kidney disease coincides with renal DNaseI shut-down in (NZBxNZW)F1 mice and in human lupus nephritis. Down-regulation of DNaseI results in reduced chromatin fragmentation and deposition of extracellular chromatin complexes in glomerular basement membranes where they appear in complex with IgG antibodies. Two objectives were regarded central in this study. First, we aimed new analyses to obtain insight into protection and repair mechanisms in lupus nephritis. The main focus in this study was to resolve whether inflammation-driving silencing of the renal DNaseI gene expression correlated with increased expression of the anti-apoptotic and survival protein tumor necrosis factor receptor-associated protein 1 (Trap1). Secondly, we aimed to translate results from murine lupus nephritis to human lupus nephritis. Mouse and human mRNA expression levels of DNaseI, and Trap1, were determined and compared with protein expression profiles and clinical data. The data demonstrate that silencing of DNaseI gene expression is highly negatively correlated with increased sessile expression of the Trap1 gene. Secondly, an acquired reduction in DNaseI appears to be important for progression of disease in both the murine and human forms of lupus nephritis. The loss of renal DNaseI seems to initiate a cascade of inflammatory signals leading to the up-regulation of repair proteins like the Trap1.

Biography

Ole Petter Rekvig completed his Ph.D. in Medical Immunology in 1981 at the University of Tromsø. He has served as professor in molecular immunology and pathology from 1984, and has served as consultant at the University Hospital from 2000. He has published scientific papers on molecular pathology and immunology with a special interest in processes linked to lupus nephritis.

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