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# Silencing of renal DNaseI in murine and humanforms of lupus nephritis imposes exposure of large chromatin fragments and activation of Toll like receptors and the Clec4e

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Recent studies demonstrate that progression of clinically silent mesangiallupus nephritis intoend-stage kidney disease is caused by an unexplained shut-down of renal DNaseIgene expression in (NZBxNZW)F1 and MRL-lpr/lprmice. Loss of DNaseIenzyme activity results in reduced chromatin fragmentation, and in deposition ofextracellular chromatin-IgG complexes in glomerular basement membranes in individuals that produce IgG anti-chromatin antibodies. The main objective of this study was to describe the biological consequences of renal DNaseI shut-down and reduced chromatin fragmentation with a particular focus on whether undigested and exposed large chromatin fragments activate Toll like receptors and the necrosis-related Clec4e receptor in murine and human lupus nephritis. Theoretically, matrix metalloproteases are also up-regulated as a consequence of Toll like receptors/Clec4e mediated activation. Mouse and human mRNA expression levels of DNaseI, Toll like receptors 7-9, Clec4e, and MMP2/MMP9 were determined and compared with in situ protein expression profiles and clinical data. According to the hypothesis, we demonstrate that exposure of chromatin significantly up-regulate Toll like receptors and Clec4e in mice, and also in patients with lupus nephritis treated with immunosuppresants.In conclusion, silencing of renal DNaseIgene expression initiates a cascade of inflammatory signals leading to progression of both murine and human lupus nephritis. Principal component analysis biplots of data from murine and human lupus nephrits demonstrate the importance of DNaseI gene shut down for progression of the organ disease.

## Biography

Elin S Mortensen has completed her Ph.D in Medical Physiology in 1991 at the University of Tromsø. Her postdoctoral studies were performed 1992-1994, also in Medical Physiology at University of Tromsø. She served as ass. professor from 2003, and professor from 2007 at Department of Medical Biology, Molecular Pathology Research Group, University of Tromsø. From 1998 she has been consultant in Clinical Pathology, University Hospital of Northern Norway. She has published scientific papers on molecular pathology of inflammation processes in cancer and lupus nephritis.

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