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Renoprotective effects of citral on accelerated and severe lupus nephritis mice by inhibiting activation signal of NLRP3 inflammasome and enhancing Nrf2 activation

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Lupus nephritis (LN) is a major complication of systemic lupus erythematosus (SLE). NLRP3 inflammasome activation, reactive oxygen species (ROS) and interstitial mononuclear leukocyte infiltration in the kidney have been shown to provoke the acceleration and deterioration of LN, although the exact pathogenic mechanism remains unclear. Development of a novel molecular pathogenesis-oriented therapeutic remedy preventing progression is clinically warranted. In the present study, Citral (3,7-dimethyl-2,6-octadienal), a major active compound in a Chinese herbal medicine Litsea cubeba was used to test its renoprotective effects in an accelerated and severe LN (ASLN) model induced by repeated injections of lipopolysaccharide (LPS) to SLE-prone NZB/Wf1 mice. The results showed that citral significantly ameliorated proteinuria, renal function and renal lesions including glomerular neutrophil infiltration, intrinsic cell proliferation, cellular crescents, fibrinoid necrosis, peri-glomerular infiltration of mononuclear leukocytes and focal tubular atrophy in ASLN mice. In the kidney, citral inhibited NLRP3 inflammasome activation and levels of ROS, NAD(P)H oxidase subunit p47phox or COX-2 and it enhanced the activation of Nrf2. In LPS-primed macrophages, citral reduced ATP-induced IL-1β secretion and caspase-1 activation but did not affect LPS-induced NLRP3 protein expression. Our data suggest that citral alleviate the mouse ASLN model by inhibiting the activation signal of NLRP3 inflammasome and increasing Nrf2 antioxidant signaling. Therefore, this type of treatment is predicted to be useful for therapy in human ASLN.

Biography

Shuk-Man Ka has completed her PhD from National Defense Medical Center, Taiwan and Post-doctoral studies from the Department of Pathology, Tri-Service General Hospital, Taipei, Taiwan and the Initiative of Gene Therapy, Harvard Medical School. She is working as an Associate Professor at the Academy of Medicine, National Defense Medical Center, Taiwan. She has published more than 45 papers in reputed journals.

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