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Lipopolysaccharide-pretreated dendritic cells ameliorate renal injury in Streptozocin-induced murine diabetes

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Plasmacytoid Dendritic Cells (pDCs) as a subset of DCs, play an important role in inducing immune tolerance, preventing allograft rejection and regulating immune responses in both autoimmune and Graft-Versus-Host Disease (GVHD). PDCs modulated by lipopolysaccharide (LPS) have been shown to be capable of suppressing experimental autoimmune encephalomyelitis. Here we investigated a possible effect of LPS-pDCs in protection against renal injury in the Streptozocin (STZ)-induced murine diabetic mellitus. pDCs derived from mouse spleen were modified *ex vivo* and stimulated with LPS (0.5 mg/ml). Mice underwent adoptive transfer with $1x10^6$ LPS-pDCs/per C57BL/6 mouse, followed by tail injection with two doses of STZ (75 mg/kg and 150 mg/kg). Mice were sacrificed at 12 weeks after STZ injection. Renal function and histopathological injury were assessed quantitatively. Kidneys from mice injected with STZ developed early symptoms of diabetic nephropathy. Transferred LPS-pDCs were found to localize to the renal cortex, but not to pancreas. Transfused LPS-pDCs accumulated progressively in kidneys up to 12 weeks after STZ. LPS-pDCs were able to protect against renal injury in STZ mice. Kidneys from diabetic mice infused with LPS-pDCs had less tubular atrophy, glomerular hypertrophy and interstitial expansion in comparison to diabetic (STZ-alone) mice. And LPS-pDCs transfusion significantly suppressed the development of interstitial fibrosis (Trichrome staining, LPS-pDCs vs STZ-alone vs Normal 0.53±0.05 vs 0.89±0.07 vs 0.09±0.004%, $p<0.01$). Numbers of leucocytes in cortex, such as host endogenous macrophages, were decreased by LPS-pDCs. On the other hand, the degree of pancreatic islet injury, as assessed by insulin staining, blood glucose and HbA1c, was unchanged after transfusion of LPS-pDCs. Our findings show that LPS-pDCs protect against renal injury in streptozotocin-induced diabetes, providing therapeutic potential in the prevention and treatment of diabetic nephropathy.

Biography

Dong Zheng is a renal researcher who graduated in 2002 from Nanjing Military College, The Second Military University in Clinical Medicine. Then he completed his Masters from The University of Manchester in the UK in 2006, where he studied the courses of Investigative Ophthalmology and Vision sciences and became interested in molecular biology. From 2007 to 2011, he was pursuing a Ph.D. in renal diseases in The University of Sydney in Australia, and particularly, in using immune cells of treating diverse types of chronic kidney diseases. He was awarded Ph.D. in May 2011. Now he works as a postdoc researcher Tongji University in China and is conducting research focusing in the treatment of renal diseases with regulatory immune cells and cellular oxidative stress on animal models.

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