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Ly6C$^+$ inflammatory monocytes regulate neutrophils inflammation response induced by lung injury

Li Liu
Sichuan University, China

Cationic liposomes administration induces severe pulmonary inflammatory response and lung injury, but little is known about the regulation of the immune response. Cationic liposomes trigger inflammation by inducing necrosis of lung cells and releasing mitochondrial DNA (mtDNA). And the activation of inflammation depends on the TLR9 and STING pathways. We show the characteristic of dynamic that Ly6C$^+$ inflammatory monocytes are recruited in Lung after the inflammatory neutrophils infiltrated in lung tissue after cationic liposomes dosing and these monocytes are required to prevent pulmonary inflammation and lung injury. We show that Ly6C$^+$ inflammatory monocytes regulate neutrophils inflammation *via* the production of prostaglandin E^2 (PGE_2), the pulmonary inflammation trigged by cationic liposomes can be controlled by PGE^2 analog treatment. IL-$10^{-/-}$ inflammatory monocytes demonstrate a previously unappreciated inflammation inhibiting function through producing PGE_2 and the effect is eliminated by indomethacin, a COX-1 and COX-2 inhibitor. Our results suggest that mtDNA and necrotic lung cells reprogramming Ly6C$^+$ inflammatory monocytes into dual phenotypes, acquiring both inflammatory and regulatory features. The findings highlight the importance of Ly6C$^+$ inflammatory monocytes in pulmonary inflammation regulation during lung injury induced by cationic liposomes.

lilyscu1990@163.com

Soluble CD52 is a potential therapeutic candidate for the treatment of myeloproliferative disorders

Maryam Rashidi, Esther Bandala-Sanchez, Yuxia Zhang, Kate Lawler, John Wentworth, James Vince and **Leonard C Harrison**
Walter & Eliza Hall Institute of Medical Research, Australia

Background & Aim: CD52 is a glycosyl-phosphatidylinositol (GPl)-anchored cell surface glycopeptide but its physiological role has not been well defined. We recently showed that cell surface CD52 suppresses T-cell function. Following activation, T-cells release CD52, which inhibits T-cell receptor signaling in bystander T-cells. In the present study, we demonstrate that soluble CD52 can induce suppression of NF-κB activation and death in innate immune cells.

Method & Results: Exposure of innate immune cells to low concentrations (10 μg per ml) of CD52-Fc potently inhibited NF-κB signaling and cytokine production in response to a range of inflammatory stimuli, including both TLR and TNFR ligands without evidence of cell death. However, at higher concentrations (30 μg/ml and above) we observed that CD52-Fc induced rapid (within 24 hours) cell death in human monocytes and mouse bone marrow-derived macrophages (BMDMs) and dendritic cells (BMDCs). Cell death was caspase-dependent because the pan-caspase inhibitor Q-VD-OPh inhibited CD52-Fc-induced cell death. In addition, high-dose CD52-Fc induced cleavage of caspases 8 and 9 and its ability to induce cell death was significantly decreased in caspase-8-deficient BMDMs. When cell death was inhibited by Q-VD-OPh, CD52-Fc still suppressed cytokine production, demonstrating that suppression of cytokine production by CD52-Fc is separable from and not due to its ability to cause cell death.

Conclusion: Our findings demonstrate that, in addition to suppressing NF-κB signaling and cytokine production, soluble CD52-Fc induces cell death in myeloid cells through the extrinsic apoptotic pathway, suggesting that CD52-Fc may have therapeutic potential for the treatment of myeloproliferative disorders.

rashidi@wehi.edu.au