REGIONAL CENTRE FOR BIOTECHNOLOGY

Seminar series

Dendritic Cell Efferocytosis-Mediated Antigen Acquisition is a Critical Mechanism for Cross-Presentation and Anti-Viral Immunity

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3:00 PM
Seminar Room

Efferocytosis is the process by which apoptotic cells are recognized and cleared in a non-phlogistic manner by phagocytic cells. Efferocytosis of apoptotic inflammatory cells has been proposed to play a critical role in inflammation resolution, and defective efferocytosis is thought to contribute to a number of maladies, including auto-immune diseases and atherosclerotic heart disease. Another critical role proposed for efferocytosis is in the uptake of virus-infected apoptotic cells leading to antigen cross-presentation to CD8+ T cells and anti-viral immunity. However, *in vivo* evidence of the importance of efferocytosis relative to other mechanisms of antigen acquisition is lacking due to incomplete characterization of the molecules DCs use to recognize and ingest apoptotic cells. We report here the identification of an efferocytosis receptor module in murine DCs comprising Axl to recognize and bind apoptotic cells, LDL receptor-related protein-1 (LRP-1; CD91) to trigger internalization of apoptotic cells, and the scaffolding protein RanBP9 to facilitate Axl-LRP-1 interaction. We demonstrate that Axl, LRP-1, or RanBP9-deficient mice infected with Herpes simplex virus-1 (HSV-1) have increased apoptotic cell accumulation, defective HSV-1 antigen-specific CD8+ T cell activation, and enhanced viral load. Human monocyte-derived and splenic DCs also utilize Axl/LRP-1 to ingest apoptotic cells. These data demonstrate a novel Axl-LRP-1-RanBP9 complex that mediates DC efferocytosis *in vivo*. These data also provide the first direct evidence that efferocytosis is a critical mechanism *in vivo* for antigen acquisition by DCs for cross-presentation and for eliciting a successful anti-viral immune response.