and orchestrates clearance of apoptotic cells to promote tolerance.

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Abstract:

Macrophages rapidly engulf apoptotic cells to limit the release of noxious cellular contents and to restrict autoimmune responses against self antigens. Although factors participating in recognition and engulfment of apoptotic cells have been identified, the transcriptional basis for the sensing and the silent disposal of apoptotic cells is unknown. Here we show that peroxisome proliferator-activated receptor-delta (PPAR-delta) is induced when macrophages engulf apoptotic cells and functions as a transcriptional sensor of dying cells. Genetic deletion of PPAR-delta decreases expression of opsonins such as complement component-1qb (C1qb), resulting in impairment of apoptotic cell clearance and reduction in anti-inflammatory cytokine production. This increases autoantibody production and predisposes global and macrophage-specific Ppard(-/-) mice to autoimmune kidney disease, a phenotype resembling the human disease systemic lupus erythematosus. Thus, PPAR-delta has a pivotal role in orchestrating the timely disposal of apoptotic cells by macrophages, ensuring that tolerance to self is maintained.