PROTECTIVE ROLE OF CONVENTIONAL DENDRITIC CELLS IN EXPERIMENTAL MODEL OF SEPSIS

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Sepsis is a life-threatening illness in which multiorgan failure results from dysregulated proinflammatory cytokine production in response to endotoxin. Dendritic cells (DCs) have been implicated in limiting the pro-inflammatory response during sepsis and improve endotoxemia tolerance. Recently, we demonstrated that activation of the aryl hydrocarbon receptor (AhR) in DCs by tryptophan metabolites is required for survival during lipopolysaccharide (LPS)-induced sepsis in vivo [1]. Whether a specific DC-subset mediated this response is unclear. To determine whether DCs are required for protection against LPS sterile sepsis we used the Zbtb46DTR mouse model, to specifically deplete DCs in vivo [2]. We found that Zbtb46DTR chimeras treated with diphtheria toxin are unable to survive sub-lethal LPS challenge compared to wild-type (WT) mice reconstituted with WT bone marrow. In addition, transfer of LPS-treated DCs into naive mice protected them from lethal LPS challenge. Notably, we found that Batf3–/– mice, which lack CD24+ DCs, are susceptible to sub-lethal LPS challenge, but mice lacking the Notch2-dependent CD11b+ DC subset are not. Our data demonstrate for the first time that CD24+ DCs are required for protection during sepsis.

1. Gargaro M. et al. (2014). Nature. 511(7508):184-90.

2. Satpathy AT. et al. (2013) Nat Immunology.14(9):937-48.