Involvement of Toso in activation of monocytes, macrophages, and granulocytes.

Rapid activation of immune responses is necessary for antibacterial defense, but excessive immune activation can result in life-threatening septic shock. Understanding how these processes are balanced may provide novel therapeutic potential in treating inflammatory disease. Fc receptors are crucial for innate immune activation. However, the role of the putative Fc receptor for IgM, known as Toso/Faim3, has to this point been unclear. In this study, we generated Toso-deficient mice and used them to uncover a critical regulatory function of Toso in innate immune activation. Development of innate immune cells was intact in the absence of Toso, but Toso-deficient neutrophils exhibited more reactive oxygen species production and reduced phagocytosis of pathogens compared with controls. Cytokine production was also decreased in Toso(-/-) mice compared with WT animals, rendering them resistant to septic shock induced by lipopolysaccharide. However, Toso(-/-) mice also displayed limited cytokine production after infection with the bacterium Listeria monocytogenes that was correlated with elevated presence of Listeria throughout the body. Accordingly, Toso(-/-) mice
succumbed to infections of L. monocytogenes, whereas WT mice successfully eliminated the infection. Taken together, our data reveal Toso to be a unique regulator of innate immune responses during bacterial infection and septic shock.