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Innate and adaptive immune response in experimental *Yersinia pestis* (Indian plague outbreak isolate) infected mice

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Yersinia pestis, causative agent of plague, is one of the deadly pathogens around the globe. Innate immune response is first line of host defense against pathogens. Once bacterium infects the host, the innate immunity provides immediate protection. Here, we have investigated innate and adaptive immune response in plague infected mice, gene expression levels of TLR1-9 and CD14, MyD88, NF-kB, TNF-α, MAPKp38, IL-1β were studied in peritoneal macrophages of plague infected mice in a time dependent manner (0 h, 24 h, 48 h, 72 h, 96 h and 120 h of post infection) by qRT- PCR. We also evaluated the immune response to Yersinia outer proteins (Yops) in Y. pestis infected mice. The genes of Y. pestis encoding virulent factors viz, YpkA, YopH, YopM, V antigen, Pla, YopN, YopJ, YopE, YopK, F1 and pH6 were amplified by PCR, cloned and expressed in Escherichia coli. To study the IgG and its isotypes level, ELISA and immunoblotting were performed using purified recombinant antigens. The major antigens recognized by murine plague infected sera were YopH, YopM, V antigen, YopE and F1 but very weak immuno reaction was observed in case of Pla. We observed a significant difference in IgG isotypes (IgG1, IgG2a, IgG2b and IgG3) to V antigen and F1, but YopH and YopE (IgG1 and IgG2b) only. We observed significant increase in the expression of CD14 at 48 h post infection, TLR4 and MyD88 at 72 h post infection in Y. pestis infected mouse peritoneal macrophages. These findings are useful for better understanding of host-pathogen interaction that lead to development of new countermeasure.

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