Immune response after intramammary infections

Invasion of the mammary gland by pathogenic bacteria triggers a battery of immune responses through interactions between a diverse array of pathogen- borne virulence factors and the immune surveillance mechanisms of the host. The adaptive immune response is initiated by antigen presenting cells (APC). Dendritic cells (DC) are the major APCs in the mammary gland and their function is crucial in the regulation of both the early innate immune responses and the subsequent adaptive immunity. Recognition and uptake of antigens at the site of infection induces maturation of the DC (Della Chiesa et al. 2005) and homing to the supramammary lymph nodes (Maymoun et al. 2012) where they present the antigen to naive T cells. Activated dendritic cells express high levels of antigen-MHC complexes, costimulatory molecules, and upregulate co-stimulatory molecules such as CD40 and B-7 molecules, all of which are necessary signals to induce and influence T cell activation and differentiation; in lactating cows, levels of IL-12 secretion has been suggested to promote Th1 differentiation. IL-12 produced by DC also induces IFN-γ production by other innate immune cells include NK cells thereby contributing to immediate pro-inflammatory responses. A predominant Th1 response results in a pro-inflammatory response, where production of pro-inflammatory cytokines results in a massive influx of polymorphnuclear cells that aim to kill the invading organisms.

Immune response after intramammary infection in late gestation

Pregnancy presents a major challenge to the maternal immune system, both in normal and pathologic states (Denney et al., 2011). The immune response is modulated to allow establishment and maintenance of a stable pregnancy without rejection. Progesterone in concentrations present during pregnancy is a potent inducer of the Th2 cytokine IL-4. A Th2 shift in pregnancy is also characterized by reduction in IL-1, TNF-α, and IL-2 producing CD4+ and CD8+ T cells (Raghupathy, 2001). Dendritic cells play a major role in immune regulation observed in pregnancy. Circulating pregnancy factors including progesterone and estrogens impact DC activation by impairing cytokine production and surface marker expression found necessary for T cell activation and Th1 differentiation, and induction of IFN-γ production in other immune cell populations. The dominant Th2 response results in a limited inflammatory response and in most cases no signs of clinical mastitis will be the result of an intramammary infection.

Discussion

As we showed earlier (Quesnell et al., 2012), lategestation inoculation with 100 cfu of E. coli results in a predictable establishment of an IMI during the last weeks of gestation. A high proportion of the initially established IMI (65%) were still present in early lactation and generally presented as mild clinical mastitis. Lategestation IMI often result in clinical mastitis in early lactation and form one of the most important challenges to reduce clinical mastitis on well-managed dairy farms. Further research in the pathobiology of IMI in late gestation and the potential interventions that would prevent or reduce such infections is important. Vaccination before late gestation, either parenteral or local may be valuable as an aid in reducing these IMI. The particular immune response dynamics it appears changes across lactation and gestation will be proof to be essential to design adequate interventions.

References

Immune response after intramammary infections in late gestation

Pregnancy presents a major challenge to the maternal immune system, both in normal and pathologic states (Denney et al., 2011). The immune response is modulated to allow establishment and maintenance of a stable pregnancy without rejection. Progesterone in concentrations present during pregnancy is a potent inducer of the TH2 cytokine system. A TH2 shift in pregnancy is also characterized by reduction in IFN-γ and IL-2 producing CD4+ and CD8+ T cells (Ragpputy, 2001). Dendritic cells play a major role in immune regulation observed in pregnancy. Circulating pregnancy factors including progesterone and estradiol impact DC activation byimpacting cytokine production and surface marker expression found necessary for T cell activation and TH1 differentiation, and induction of IFNγ production in other immune cell populations. The dominant TH2 response results in a limited inflammatory response and in most cases no signs of clinical mastitis will be the result of an intramammary infection.

Discussion

As we showed earlier (Queensfield et al., 2012), lactationgestation inoculation with 100 cfu of E. coli C1 results in a predictable establishment of an IMI during the last weeks of gestation. A high proportion of the initially established IMI (65%) were still present in early lactation and generally presented as mild clinical mastitis. Lactation-gestation IMI often result in clinical mastitis in early lactation and form one of the most important challenges to reduce clinical mastitis on well-managed dairy farms. Further research in the pathology of IMI in late gestation and the potential interventions that would prevent or reduce such infections is important. Vaccination before late gestation, either prenatal or local may be valuable as an aid in reducing these IMI. The particular immune response dynamics as it changes across lactation and gestation will prove to be essential to design adequate interventions.

References


Figure 1: Activation of the immune response in Mammary Epithelial Cells. E. coli induces the expression of the three master cytokines IL-1, TNFα and IL-6. S. aureus only drives IFNγ expression via a MyD88 independent signal transduction.