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Probiotic *Lactobacillus acidophilus* strain NP51® Curtails the Progression of *Mycobacterium avium* Subspecies *paratuberculosis* (MAP) Infection in Balb/c mice

A.S. Leaflet R2597

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Summary and Implications

We evaluated the preventative effects of *Lactobacillus acidophilus* strain NP51 fed to Balb/c mice infected with a virulent strain of *Mycobacterial avium* subspecies *paratuberculosis* (MAP) isolated from a clinical cow at the National Animal Disease Center in Ames, Iowa. Mice were randomized to treatment groups that were fed either viable- or heat-killed NP51 and inoculated with either viable- or heat-killed MAP or sterile phosphate-buffered saline. Feeding the NP51 elevated numbers of T lymphocytes in the spleen and increased the concentration of interferon-gamma (IFN-γ) in the supernatant of splenocytes stimulated *in vitro* with MAP antigen. Most importantly, feeding the NP51 lowered the number of viable MAP CFU in the livers of infected mice on day 180 of the study. These results suggest that feeding the NP51 to BALB/c mice has potential to prevent the advance of MAP infection in mice.

Introduction

*Mycobacterium avium* subspecies *paratuberculosis*, the causative agent of Johne’s disease (JD), is known to infect domestic ruminants such as cattle, sheep, goats, camelids, and other free and captive species worldwide. Johne’s disease is characterized by development of granulomatous enteritis, profuse watery diarrhea, and progressive wasting. In the US, JD is prevalent in about 68% of US dairy herds. Associated losses to the US dairy industry are approximately $250 million annually. Economic losses result from decreased reproductivity, feed efficiency, and milk production, early culling, and death of cattle. However, milk production losses in subclinically and clinically infected cattle, are the most alarming.

Materials and Methods

Balb/c mice (190 females and 190 males) were assigned randomly to one of ten treatment groups: sentinel, control, heat-killed MAP, viable MAP, heat-killed NP51®, viable NP51®, heat-killed NP51® plus heat-killed MAP, heat-killed NP51® plus viable MAP, viable NP51® plus heat-killed MAP, viable NP51® plus viable MAP. Mice were fed $1 \times 10^8$ CFU of NP-51® mice$^{-1}$ day$^{-1}$ mixed in standard mouse chow starting on d 1 of the study. Mice were challenged with $1 \times 10^8$ CFU of MAP injected intraperitoneally on d 45. Subsequently, ten mice from each treatment group were euthanized on d 45, 90, 135, and 180 of the study. Mice body weights were recorded weekly. Fecal samples were collected on two separate days and composited weekly. Blood samples were withdrawn by cardiac puncture and sera were used to quantify IgG and IgA. In addition, spleens, ceca, ilea, livers, and mesenteric lymph nodes (MLN) were dissected and cultured to determine MAP burden in tissues. Also, the effect of NP51® on tissue histopathology was examined by staining tissue slides with H & E and Ziehl-Neelsen stains. Splenocyte single cell suspensions were stimulated with MAP antigen for examination of T cell differentiation and secretion of cytokines.

Results and Discussion

Feeding either the heat-killed or viable NP51 to mice challenged with the viable MAP decreased ($P = 0.0001$; Figure 1) the cellularity of their spleens on d 180 of the study compared with that of the infected control (VM). In addition, MAP burden in CFU/g was decreased ($P = 0.01$; Figure 2) in the livers of mice fed either the heat-killed or viable NP51® compared with that of the infected control (VM). Taken together, these data suggest that feeding the probiotic NP51 to mice infected with MAP induces immune responses that aid the elimination of MAP in vivo and curtail the progression of the infection in Balb/c mice.

Acknowledgments

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Figure 1. Splenocytes numbers on d 180 in spleens of mice fed chow plus maltodextrin (control), chow plus maltodextrin and challenged with heat-killed MAP (HM), chow plus maltodextrin and challenged with viable-MAP (VM), chow plus heat-killed NP51 (HNP), chow plus HNP and challenged with heat-killed MAP (HNP+HM), chow plus HNP and challenged with VNP (HNP+VM), chow plus viable-NP51 (VNP), chow plus VNP and challenged with the HM (VNP + HM) or chow plus VNP and challenged with the VM (VNP + VM).

Figure 2. MAP burden on d 180 in CFUs/g of livers of mice chow plus maltodextrin and challenged with viable-MAP (VM), chow plus HNP and challenged with VM (HNP+VM), or chow plus VNP and challenged with the VM (VNP + VM).